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A Panel Discussion

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C.M.A. Annual Meeting, April 30-May 3, 1950, San Diego

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What's New in Pediatrics

Communicable Diseases

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CHEMOTHERAPEUTIC AGENTS

EACH new chemotherapeutic agent which makes its appearance on the medical horizon is welcomed eagerly. It is used many times, unfortunately, with careless abandon. All are double-edged swords, healing when correctly used, jeopardizing when misused. Information regarding toxic manifestations is available only after careful observations honestly recorded.

Penicillin, now the elder brother of the antibiotics, is used so widely that it is wise to be reminded that this relatively harmless, non-toxic agent does produce untoward reactions. These may be immediate or Herxheimer-like with shock and death, or they may be delayed, causing discomfort to both patient and physician. Frequently, allergic reactions are observed, namely, urticaria, laryngeal edema, fever, dermatitis *Exfoliativa*, neuritis, exacerbations of epidermophytosis and epidermophytids, and dermatitis venenata, when the drug is used topically.

Streptomycin is one of the antibiotics which early was considered to be comparatively innocuous. Time and use have decided otherwise. Many reports of toxic reactions are appearing in the literature. The most constant untoward manifestation recorded is temporary or permanent impairment of the function of the eighth nerve. Fever, dermatitis, eosinophilia, pruritus, conjunctivitis, and local irritation at the site of injection have been noted singly or in combination in the use of this agent.

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Presented as part of a Panel Discussion on What's New in Pediatrics before the Section on Pediatrics at the 78th Annual Meeting of the California Medical Association, Los Angeles, May 8-11, 1949.

In the communicable disease unit of the Los Angeles County Hospital it has been noted, on many occasions, that when streptomycin is given intrathecally (in tuberculous and influenzal meningitis) patients develop an immediate shock-like picture with cyanosis, rapid pulse, coma, opisthotonus, within a few minutes after administration. This has occurred sufficiently often to cause serious consideration of abandoning intraspinal use of streptomycin in influenzal meningitis.

Beham² and associates (New York) reported three cases of painful, erosive, membranous stomatitis involving the entire oral mucous membrane as well as the undersurface of the tongue. When the drug was discontinued the lesions disappeared in 14 days. Retreatment caused a rapid appearance of the lesions.

Hunnicutt⁷ and associates reported a fatal case of toxic encephalitis caused by streptomycin. McCullough¹³ and co-workers, in the treatment of brucellosis with the combined use of sulfadiazine and streptomycin, report two cases of severe encephalopathies. These occurred within a few hours after the first dose of streptomycin. They feel that the toxic effects on the nervous system have been frequent enough, when the two drugs are used in combination, to warrant considering the possibility that the combined use of the drugs increases both toxicity and clinical effectiveness. They recommend that such treatment be reserved for the seriously ill. (Toxic dermatitis develops in physicians and nurses handling this drug constantly.)

Aureomycin is one of the newer antibiotics derived from a strain of *Streptomyces aureofaciens*. It is a crystalline hydrochloride salt soluble in distilled water, less soluble in isotonic saline solutions. These

solutions are acid with a pH of 4.5. The drug deteriorates rapidly at room temperature in alkaline solution. It is bacteriostatic and bactericidal, the latter only in high concentrations. Herrell⁵ at the Mayo Clinic has shown that aureomycin is readily absorbed in the general circulation. After a single oral dose of 0.75 gm. to 1 gm. the serum content of the drug rapidly approaches therapeutic levels. A constant level is maintained for several hours. There may not be complete disappearance from the serum for 24 to 30 hours. When 0.75 gm. to 1 gm. was given orally every six to eight hours, the serum concentration varied between 2 and 4 micrograms, or, on occasions, 8 micrograms per milliliter. These studies also showed that aureomycin diffuses into the spinal fluid in amounts that may be effective, into the pleural fluid, and through the placenta into the fetal circulation. It is excreted in large amounts in the urine and bile. Too, it is found in the kidneys, liver, lungs and spleen.

Aureomycin stands as a signpost pointing in three directions, giving promise of showing the way toward conquest of a large variety of Gram-positive and Gram-negative bacteria, the rickettsial diseases, and virus infections of the psittacosis-lymphogranuloma venereum group.

Aureomycin is usually given orally in doses of 50 mg. per kilogram of body weight per 24 hours, in divided doses given at intervals of two to six hours. To date the toxic effects have been minimal. Nausea, vomiting, and cystitis may occur due to the acidity of the drug.

Chloromycetin is obtained from cultures of the species *Streptomyces venezuelae*. Also, it can be prepared synthetically. It promises to be the most valuable therapeutic agent in the treatment of typhoid fever, typhus fever, scrub typhus, Rocky Mountain spotted fever, brucellosis, and bacillary urinary infections as well as in primary atypical pneumonia. It would appear to be relatively non-toxic to humans. High blood levels have been found within 30 minutes after oral administration, and appreciable amounts in the urine in the same period of time. The usual dosage is 50 to 60 mg. per kilogram of body weight initially and then 0.25 gm. every two to four hours.

Garlicin, a new antibiotic, is extracted from garlic. In a study made by Machado¹² and associates the drug was shown to inhibit growth of the colon bacteria. Its activity is enhanced by the sulfonamides. When taken orally it is found in the blood; it diffuses into spinal fluid and it is eliminated in bile and urine. It is found in the latter in two hours after administration. It is non-toxic even when given in doses up to 700 times the maximal therapeutic dose. In the treatment of 300 patients with enteric infections, it was found that those with *Shigella* infections showed improvement on the second day and bacteriological cure in six days. The average total dose was 332 units over the period of six days. In *Salmonella* infections, including paratyphoid, there

was improvement on the second or third day and cure in nine days. The average dose for the latter period was 363 units. Stools of 31 out of 35 patients with amebiasis became and remained negative with an average total dose of 550 units over 10.3 days.

BAL—Furmanski⁶ of Birmingham Veterans' Hospital made a most interesting report on the use of this drug in the treatment of four patients with peripheral neuritis of infectious origin. The BAL used was 10 per cent solution of 2, 3-dimercaptopropanol with 20 per cent benzyl benzoate and peanut oil as the vehicle. It was given by injection once daily for 9 to 22 days. The dose was 1.5 mg. to 3 mg. per kilogram of body weight per day. Response to treatment was rapid. The author postulates that the "mode of action in these cases may be similar to that of the heavy metal intoxications, i.e., conjugation of a toxin or toxic metabolite which had inactivated the enzyme systems. It is also possible that in the cases of infectious origin BAL inhibits one of the essential enzyme systems of the virus and aids the cell in overcoming the invasion."

ASPECTS OF TREATMENT OF SOME OF THE COMMUNICABLE DISEASES

Brucellosis, a disease which may be acute, subacute, or chronic, was one of the first infectious diseases for which Koch's postulates were established; yet it remains a therapeutic enigma to clinicians in spite of a vast array of chemotherapeutic agents available. Gradually, however, data are being assembled with respect to the relative merit of the individual drugs and antibiotics so that thinking may be clarified about its treatment in the near future.

Dr. A. G. Bower, for many years chief consultant for and chief of staff of the communicable disease unit of the Los Angeles County General Hospital, has had wide experience in treatment of brucellosis. He emphasizes that the proper, intelligent use of the sulfa drugs will effect cures that are permanent. In his own words: "When no contraindication exists, and when the patient has never been treated previously with any of the sulfonamide drugs, treatment with sulfonamides has never failed to effect a cure in our clinic. Conversely, when patients have been given sulfonamide drugs in doses insufficiently large to effect a cure at some time before we have seen them, in no single instance have we ever subsequently cured a case with these drugs. The secret lies in maintaining accurately titrated high blood levels of sulfadiazine or sulfanilamide constantly present for a period of two weeks. This is a hospital procedure. The level is maintained at 15 mg. per cent or higher, and in those patients not making progress after several days of continued observation, fluids are carefully restricted for a day or two to increase the sulfa-levels in the blood. The reason these drugs fell into disrepute in the treatment of this disease was because doses were inadequate, blood levels were not ascertained and controlled, the patients were not hospitalized, and the treatment was

not continued long enough. If you are not successful in the first attempt, or if treatment has to be interdicted, it is useless ever to try it again."

Spink¹⁷ and his associates in a report on 35 patients with brucellosis, nine of whom were treated with sulfadiazine and streptomycin, expressed the opinion that the combination was more effective than either agent used alone. Three of these nine patients had the chronic form of the disease, with manifestations of infection for three months or more. Spink recommended that streptomycin be given intramuscularly in doses of 0.5 gm. every six hours for seven days. Sulfadiazine should be initiated simultaneously with a dose of 4 gm. and then 1 gm. every four hours for at least two and preferably three weeks.

Herrell and Barber⁶ of the Mayo Clinic recently reported that the combined use of aureomycin and dihydrostreptomycin appears to be the most effective method of treatment for brucellosis. Heilman of the department of bacteriology of the Mayo Clinic also found these drugs in combination to be the most effective method of treating *Brucella* infection in mice. Many combinations were tried—chloromycetin and sulfonamide, chloromycetin and aureomycin, chloromycetin and dihydrostreptomycin—as well as chloromycetin alone. None were as effective as aureomycin and dihydrostreptomycin. The recommendation for treatment is the administration of 3 gm. of aureomycin daily by mouth together with the simultaneous administration of 2 gm. of dihydrostreptomycin per day by the intramuscular route. In acute brucellosis the course of treatment should be 12 to 14 days. This method of treatment has the advantage of causing very little inconvenience to the patient. Also, possibility of toxic manifestations are minimized inasmuch as singly or together the two drugs, aureomycin and dihydrostreptomycin, are less toxic than when regular streptomycin alone or sulfadiazine alone, or the two in combination are used.

According to Parke, Davis and Company six patients with brucellosis, five of whom had positive blood culture, were successfully treated with chloromycetin with an average total dose of 17.5 gm. per patient. The average duration of fever was 2.4 days. On the basis of this it has been recommended that the patient with acute brucellosis be given an initial dose of 60 mg. per kilogram of body weight and 0.25 gm. every three hours thereafter for at least two and preferably three weeks.

Typhoid fever. Before the use of typhoid bacteriophage, more particularly type-specific phage, the treatment of this disease usually consisted of general supportive measures or occasionally immuno-transfusion. Typed phage has established itself as an effective mode of treatment of this entity.¹⁰ In the recent past it has been responsible for lowering the mortality rate of 5 per cent in the communicable disease unit of the Los Angeles County General Hospital.

Since the advent of chemotherapy, each new drug

and antibiotic has been used upon its appearance, in the treatment of typhoid fever with hopeful expectancy. All have failed except chloromycetin. From all indications, chloromycetin appears to produce the desired effect within a very short period of time, and with no toxic side-reactions.

Woodward, Smadel and associates¹⁹ reported ten cases of typhoid fever treated with chloromycetin with cure in all, even in one patient with massive intestinal hemorrhage and in another with intestinal perforation. The drug was given orally with an initial dose of 50 mg. per kilogram of body weight and 0.25 gm. thereafter every two hours until the temperature was normal; this same dose was given every three to four hours during the first five days of normal temperature. Improvement was noted in 24 hours. The average duration of fever after treatment was started was 3.5 days. There were two relapses after 10 to 16 days without fever; however, in these cases the patients responded well to the second course of the drug, no lack of sensitivity to the drug having occurred.

During March of 1949, two children acutely ill with typhoid fever were treated with chloromycetin in the communicable disease unit. One patient, an 11-year-old girl, received 3 gm. daily by mouth for six days, and then 1 gm. daily for four more days. Within 36 hours after starting treatment there was clinical improvement and in 72 hours the temperature dropped by crisis from 103°F. to 96°F. The second child was one year of age. She received 3 gm. daily by mouth for three days and 1.5 gm. each day thereafter for four days. Clinical response was almost the same as in the first instance, but in this case the temperature was normal in 48 hours.

Typhus fever. During the summer of 1948 nineteen patients with murine typhus were treated with aureomycin in Mexico. Observations were made by a group of investigators from the University of Guadalajara and the New York Hospital-Cornell University Medical College. Response to treatment was spectacular and recovery uniformly occurred by crisis. The average duration of fever was 1.7 days after starting therapy regardless of the day of illness on which the treatment was begun. There were no relapses in spite of the fact that seven of the patients were treated for only one or two days. Convalescence was uneventful. From observation, the investigators felt that the "lowest full effective dose was somewhere between 50 and 100 mg. per kilogram per day for a short interval of therapy." All patients, with the exception of one, received the drug orally. One patient was given aureomycin intravenously in doses of 200 mg. at eight-hour intervals during the first 24 hours and then at 12-hour periods on the second day. Improvement was so rapid that when the last dose (fifth) was given, the patient was completely asymptomatic as well as afebrile. There were no evident toxic reactions.

In November and December of 1947, in the province of Camacho, Bolivia, during an epidemic, Payne, Knaudt, and Palacios¹⁴ treated patients suf-

fering from typhus fever with chloromycetin. Improvement was dramatic. One patient, 18 years of age, who on the third day of illness was extremely toxic and stuporous, was given 1.5 gm. of the drug by mouth once daily for two days. Fever and symptoms were gone on the second day. The patient was discharged on the fourth day. The investigators found that chloromycetin was safe for intravenous use when given in doses of 10 mg. per kilogram of body weight for three days. They found that headache and vision began to improve ten minutes after the intravenous injection was finished. Oral administration was just as effective; but then eight to twelve hours were required before results were evident.

Rocky Mountain spotted fever, an infectious disease caused by *Rickettsia rickettsii* and transmitted by the bite of ticks, first observed in the western section of the United States, now has been reported from every part of the country. It is a disease with acute fulminating symptoms, an incubation period of seven days, and is characterized by a hemorrhagic macular or confluent rash of the entire body. The mortality rate may vary between 10 and 50 per cent. Prior to para-aminobenzoic acid, with the exception of hyperimmune rabbit serum, the treatment was chiefly symptomatic and supportive.

Tichenor and co-workers¹⁸ of Washington, D. C., reported eight patients treated with para-aminobenzoic acid with no deaths, as compared with a 10 per cent death rate in a control group. The dose schedule followed, in children, was 0.33 to 0.5 gm. per pound of body weight per 24 hours given at two-hour intervals; and, for adults, 6 gm. as an initial dose and 4 gm. at four-hour intervals. Treatment with the drug was continued for seven days, or, for approximately two to four days after temperature reached normal. There was a suggestion of liver dysfunction by changes produced by cephalin flocculation tests and prothrombin times.

Very encouraging results with aureomycin were reported by Ross and co-workers¹⁹ in 13 cases treated since June, 1948, in Washington, D. C., and Baltimore. The maximum dose of the drug given was 5 mg. per kilogram of body weight at hourly and then two-hour intervals until the temperature reached normal, after which time it was given every four hours for a period of 48 hours. The average period of treatment was six days. There were no relapses and no toxic symptoms or signs. There were no deaths and the average hospital stay was eight days. Aureomycin is preferred to para-aminobenzoic acid because it is clinically more rapidly effective and because of absence of liver and kidney damage.

Pincoffs and associates¹⁵ treated 15 patients with chloromycetin. Quite dramatically the temperature dropped to normal in 76 hours after the initial dose. Symptomatically there was some improvement in the first 24 hours with pronounced diminution of headache, etc., in 48 hours. It is recommended that the initial dose be 60 mg. per kilogram of body

weight, then 0.25 gm. every three hours until the temperature remains normal for 48 hours.

Q fever is a disease caused by *Coxiella burneti*, closely related to the *Rickettsia*. It tends to occur endemically in the milkshed area of Los Angeles County. The disease usually has an abrupt onset either with rhinoconjunctivitis, or severe headache with retro-orbital pain followed by blood-tinged sputum, and chest pain. The leukocyte count may be normal or slightly elevated. Complement fixation tests usually do not show positive reaction until the third week.

During the past year in the communicable disease unit two patients who had this disease were treated with streptomycin and two with aureomycin. One 30-year-old male with history of illness of four or five months' duration received 2 gm. of streptomycin daily, or 0.5 gm. four times per day for six days. The temperature, which had varied between 103°F. and 104°F. dropped to normal on the fourth day. The patient remained symptom-free and afebrile thenceforth. Complement fixation was in dilution of 1:1,024. The second patient, a male 53 years of age, received streptomycin in doses of 2 gm. daily for five days. On the second day of treatment the generalized body pains and throbbing headache disappeared. The third patient, a man of 36 years, received aureomycin in doses of 500 mg. four times a day for six days. The temperature promptly dropped from 103°F. to normal, and clinical symptoms subsided in three days. The fourth patient with Q fever was a man 36 years of age who received 1,000 mg. of the drug four times a day for nine days. The temperature reached normal in three days and the patient was completely asymptomatic in 24 hours.

Tularemia stands out as one disease in which streptomycin is unequivocally indicated. The clinical effect is prompt and usually dramatic. Fever is down on or before the third day; the headache, malaise, mental depression are gone in 24 hours. Within 24 to 48 hours buboes decrease in size, and ulcers show signs of healing. In pneumonic tularemia, which previously carried a mortality rate of 20 to 40 per cent, the curative value of the drug is most spectacular. In severe primary atypical pneumonia, where tularemia may be etiologically suspected, a therapeutic trial with this drug may be life-saving. Inasmuch as streptomycin does not inhibit appearance of diagnostic agglutinins there would be no reason for withholding the drug.

Since the advent of streptomycin, three patients with tularemia have been treated with the drug in the communicable disease unit. One man, aged 37, with the ulceroglandular type, had been ill for one week before entry and the temperature spiked daily to 103°F. before streptomycin was given. The patient had a normal temperature and was clinically asymptomatic in 36 hours after starting treatment. He was given a total of 8 gm. in divided doses over a four-day period. The remaining two patients were husband and wife. Both gave history of chills, fever,

and development of an ulcer on the hand four days after dressing wild rabbits. The man, aged 55, had the ulceroglandular type only. He was given 1.6 mg. of streptomycin over a four-day period. Temperature was normal eight hours after the first dose and there was pronounced evidence of healing of the ulcer with disappearance of the glandular enlargement on the fourth day. The wife, aged 63, had pneumonic involvement in addition to an ulcer on the right thumb. She was given a total of 2.2 gm. of streptomycin over a four-day period. The temperature dropped from 103°F. to normal in 24 hours. The pneumonia was gone and there was almost complete healing of the ulcer by the fourth day. The small doses used in these two cases were not a matter of choice but of necessity because of the difficulty in obtaining the drug at that time.

Actinomycosis involving the central nervous system is considered to be fatal in all cases. Thus, Jacobson and Cloward's⁸ report of a case of actinomycosis meningitis with recovery is received with enthusiasm. This patient had signs of mental illness for 18 months before onset of acute signs of meningitis. The latter was diagnosed positively by the finding of *Actinomyces* in the spinal fluid. After two months of intensive treatment with penicillin, sulfadiazine, and streptomycin the patient was discharged from the hospital completely recovered from mental illness as well as the meningitis. There has been no evidence of relapse. Although all three drugs were used simultaneously, the patient first began to show signs of improvement when streptomycin was added. The latter was given intramuscularly and intrathecally, a total of 26 gm. in six days.

Arnold and Austin¹ in Hawaii reported cure of actinomycosis of the jaw with Diasone® (disodium formaldehyde sulfoxylate diamino-diphenylsulfone). The drug was given orally in accordance with the dose used by Dr. Fernando Latapi of Mexico City, who observed that the drug cured three patients. The dose used was that employed in Mexico in the treatment of leprosy: 1 gm. daily for the first week, 1.3 gm. (20 grains) daily for the second week and 1.6 gm. daily thereafter. By the end of the fourth week there remained only a residual fibrotic nodule less than one-sixth the size of the original mass.

Pertussis is one of the most serious of the acute contagious diseases of childhood and results in more deaths in children under two years of age than diphtheria, measles, scarlet fever and poliomyelitis combined. Early diagnosis, efficient nursing care and intelligent medical supervision, together with the use of the sulfa drugs, penicillin, and hyperimmune pertussis serum have helped diminish the deadliness of this scourge.

Because of its effectiveness against pertussis organisms in vitro, streptomycin was used in treatment by Gordon⁴ and co-workers in a controlled series (27 treated and 28 controls) of cases. It should be noted that 23 of the 27 patients treated were under eight months of age. The dose of the drug was 25 mg. per pound of body weight per 24

hours. This daily total was divided by eight and given intramuscularly every three hours for an average of seven days. Some improvement was noted in 24 to 48 hours. Definite improvement occurred in three to four days. Mortality in the control group was 39.3 per cent as compared with 7.4 per cent in the treated group, but there was no significant improvement in the length of hospitalization when the two groups were compared.

The aerosol route of administering streptomycin is reported as most satisfactory by Leichenger and Schultz.¹¹ One gram of the drug was dissolved in 8 cc. of normal saline solution; 1 cc. of this was given every three hours. The solution was nebulized by attaching a Vaponefrin nebulizer to an oxygen tank, and administered via an infant-sized nasal mask (B.L.B.). The rate of flow of oxygen was 4 to 6 liters per minute and the average period of time to administer an aerosol dose of streptomycin was from 7 to 10 minutes.

In the communicable disease unit the triple use of hyperimmune pertussis serum (Cutter's Hyperpertussis), sulfamerazine and sulfadiazine in combination, and penicillin, has proved efficient, and streptomycin has been reserved for patients who are not making the usual satisfactory response. During 1946 the mortality rate was 3.7 per cent and in 1947 to 1948 it was 2.8 per cent, or an average of 3.2 per cent for the two-year period. This is an excellent death rate considering that about 80 per cent of the patients were under two years of age and over 50 per cent had complications on entry.

To cure a disease is praiseworthy; to prevent it is a finer accomplishment. There is no longer any valid excuse for postponing immunization for pertussis. It can be instituted on the first day of life, if desired. Certainly it should not be delayed beyond the third or fourth month. Because of studies made and others in process more doctors are giving not only pertussis immunization but combined immunizations at earlier ages than the time-honored six months. For the past three years it has been the practice of the author routinely to commence immunization with the combined antigens (alum precipitated diphtheria, pertussis and tetanus toxoid) at three months of age, giving three injections at four to six-week intervals and following with a booster injection within six to nine months. Amazingly few reactions are encountered.

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All That Queries is Not Queensland

As a mother with a defective child, many writers on medical subjects appear determined to bring to maturity the erroneous assumption that the "Q" in *Q fever* indicates the place in which the disease entity was first noted—Queensland, Australia. Indeed, so plausible is the error that glib reference to "Q (for Queensland) fever" persists in medical writing despite sound evidence that, had it not been for accidental geographic-pathologic coincidence, the "Q" might (confoundingly) have stood for, say, New South Wales.

Lennette made some effort to right the wrong in an article titled "Q Fever in California" which appeared in the August 1948 issue of CALIFORNIA MEDICINE. In a footnote to that article, Lennette said that he had had from Derrick, who first described the features of the disease as it appeared in Queensland, a personal communication to the effect that "Q" was not for Queensland but for "query" because of uncertainty as to identification. Queensland, it seems, was implicated merely because it was known to have been at the scene of the investigation.

It is to be hoped that, with this further admonition, medical writers will mend their ways p.d.q. (for quickly).

What's New in Pediatrics

Rheumatic Fever

ROBERT G. SHIRLEY, M.D., *Beverly Hills*

THE seriousness of the rheumatic fever problem has at long last been recognized. Public-spirited organizations and the medical profession have joined hands in a concerted effort to procure funds for research and for the dissemination of the knowledge already accumulated on the symptomatology, diagnosis and treatment of rheumatic fever. In 1948 there were 22 state and 22 private rheumatic fever programs.

Angove¹ reported that rheumatic fever kills more than five times as many persons annually as poliomyelitis, pertussis, diphtheria, scarlet fever, measles and meningitis combined. For every case of poliomyelitis in the age group 5 to 15 years there are 111 cases of rheumatic fever, and for every death from poliomyelitis there are 154 deaths from rheumatic fever.

Martin¹⁰ has estimated that each year 40,000 persons die from rheumatic fever and its sequelae in the United States, and that between 800,000 and 1,000,000 new cases develop annually. Rheumatic fever ranks first as a cause of death for girls in New York City and is second only to accidents for boys.

Meakins¹² found the disease seven times more common in urban than in rural school populations. The disease is about 20 times more common in the working class than among the wealthy. There is a pronounced seasonal variation coinciding with the prevalence of hemolytic streptococcus infections. At one time it was felt that rheumatic fever was a disease of the temperate zone. We now know it has a universal distribution, but occurs less commonly and is generally less virulent in subtropical and tropical areas where streptococcal infections are not as prevalent. Clark³ observed no cases of mitral stenosis during 30 years in the tropics. He found 747 cases of joint involvement and other manifestations, obviously rheumatic, but no rheumatic heart disease. These data were gathered from observation of 571,526 clinic outpatients drawn from an estimated population of 33,748,369.

Coburn and Moore⁴ have expressed the opinion that there are three factors in the genesis of the rheumatic state:

1. A constitutional factor transmitted as a single autosomal recessive gene—a conclusion reached by Wilson and Schweitzer²² based on the quantitative agreement between the observed incidence and the

value predicted from this hypothesis. The presence of this recessive gene alters the host in some manner as yet unknown, to make him constitutionally susceptible. It has been estimated that about 5 per cent of the population are so affected. The onset of rheumatic fever in this susceptible 5 per cent of the population depends on the two other factors, namely:

2. Infection with the hemolytic streptococcus, whose products precipitate the rheumatic attack, and

3. Deficiency in the host of certain dietary factors.

Cavelte² has recently carried out some interesting experimental studies supporting the generally accepted belief that the rheumatic process is initiated by the hemolytic streptococcus. He found that non-antigenic emulsions of homologous heart muscle and connective tissue can be rendered antigenic for rabbits by combining them with heat-killed hemolytic streptococci. Such a mixture when injected into rabbits produced valvular endocarditis with inflammatory infiltration and proliferation. Mixtures of skeletal muscle, free from connective tissue, and hemolytic streptococci did not produce cardiac lesions. Cavelte found antibodies to human heart in titers of 1:40 to 1:320 in 47 out of 67 samples tested from patients with rheumatic heart disease. On the basis of these studies Kerr⁹ suggested that the hemolytic streptococci or their products, in conjunction with the connective tissues of the body, produce auto-antibodies which are the cause of the lesions associated with the rheumatic state. Previously, Rich and Gregory¹⁵ produced lesions in laboratory animals similar to those of rheumatic carditis by inducing anaphylactic hypersensitivity to sulfonamides. They later produced widespread vascular lesions similar to rheumatic arteritis, lupus erythematosus and periarteritis nodosa by anaphylactic hypersensitivity. These studies are additional evidence supporting the role of the factor of hypersensitivity in rheumatic fever.

The importance of the diet in the pathogenesis of rheumatic fever is not clearly understood. Coburn and Moore⁴ found that children with recurrences were lacking in proteins, iron, vitamin A and possibly calcium and riboflavin.

Jackson and co-workers,⁸ from a study of rheumatic subjects receiving supervised diets and environmental care, concluded that if the disease is definitely inactive, adequate diet and good care will practically eliminate the chances of recurrence with

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carditis. They found that the degree of deficiency of the diet was related to the incidence and degree of cardiac damage.

Van Breeman, cited by Coburn and Moore,⁴ reported that in the Netherlands there were only 228 deaths from rheumatic fever between the years 1920 and 1925. In the industrial cities of England it was a very important cause of death. The climate, race, age and incidence of respiratory infections were about the same in the two countries. The major difference was in the diet, the people of the Netherlands receiving abundant amounts of dairy products. The role of the diet is difficult to evaluate, however, as the increased incidence of rheumatic fever in the group on an inadequate diet may be due to an increased susceptibility to infections.

Griffith⁶ has divided the rheumatic cycle into four phases:

1. The phase during which the patient is host to the hemolytic streptococcus. Swift¹⁸ is of the opinions that if all cases of rheumatic fever could be studied bacteriologically and immunologically for the presence of antibodies against streptococcal components, practically all would be shown to have a "Phase 1" prior to the attack of rheumatic fever. The site of the infection is generally believed to be in the upper respiratory tract and the offending substance is probably produced locally.

2. The latent phase which lasts from one to four weeks. This is one of the most characteristic features of this disease. It is during this period that the immunologic reactions are becoming established.

3. The period of rheumatic activity during which the classical symptoms of rheumatic fever occur, and

4. The period of rheumatic inactivity. The fourth period may be the end to the rheumatic process or may be followed by one or more recurrences.

Much emphasis has been put on the major and minor criteria of rheumatic fever in recent years. Although there have been minor differences of opinion, the consensus is that carditis, subcutaneous nodules, erythema marginatum, polyarthritis, chorea and a history of a preceding attack are the major criteria. Fever, abdominal pain, precordial pain, non-traumatic epistaxis, weight loss, tachycardia and pneumonitis are listed as the important minor criteria.

Such a division of symptoms is of value in bringing to mind the important features of the disease. It is not without danger, however, to dictate strict standards of diagnosis which depend on a specific number of major and minor criteria being present. The ability to evaluate the material at hand comes only after years of intimate contact with rheumatic patients. One need only to make rounds on any rheumatic fever service or attend any cardiac clinic to realize, from the differences of opinion expressed by those who helped formulate the criteria, that such a punch-board method will never work in the diagnosis of rheumatic fever any more than it has

worked in the diagnosis of any other disease. The major and minor criteria are aids in diagnosis, nothing more.

The electrocardiogram, erythrocyte sedimentation rate and x-ray remain the chief laboratory procedures used in the appraisal of the child suspected of having rheumatic fever and in directing therapy during the period of activity. The most frequent changes in the electrocardiogram are an increase in the PR interval, changes in the QRST or ventricular portion of the electrocardiogram, and disturbances of rhythm. Frequently repeated electrocardiograms are important in the proper evaluation of any deviation from normal. A change in the electrocardiogram during the period of observation is more important in indicating rheumatic activity than the existence of any specific variation from the accepted normal.

Recently Taran^{19, 20, 21} has emphasized the importance of the Q-T quotient as an indication of rheumatic activity. The Q-T interval is the duration of electrical systole, and its use as an indication of cardiac function is based on the physiological principle that a disturbance in the time relationship of systole and diastole is a manifestation of impairment of the functional integrity of the myocardium. When electrical systole is prolonged the diastolic period or perfusion time of the heart muscle is shortened. This results in local tissue anoxia and ultimate heart failure.

The erythrocyte sedimentation rate should be used with caution in the diagnosis of rheumatic fever. There is a tendency to attribute undue importance to this laboratory procedure. It should be evaluated in the light of the history, physical findings and other laboratory data. It is more useful and more reliable as a guide in the management of the rheumatic patient, but even here it is sometimes misleading in either direction.

An x-ray of the chest for heart size is valuable as a base line for future comparison. Schwedel¹⁷ has expressed the belief that progressive cardiac enlargement or the enlargement of an individual cardiac chamber as compared to a previous film is an indication of rheumatic activity. The chambers most commonly enlarged are the left auricle and the right auricle and ventricle. Pulmonary complications and pancarditis are not uncommonly encountered and roentgen study then is needed for confirmation of the clinical impression. It must again be emphasized that this is just another aid in the diagnosis and treatment and should not in any way supplant a careful history, detailed physical examination and the other laboratory procedures of value in the appraisal of the child with rheumatic fever.

MANAGEMENT

Bed rest continues to be the cornerstone in the management of the child with rheumatic fever. It is unfair to follow any set rule for the period of complete bed rest. Each case should be judged

individually. But bed rest should by all means be continued until all signs of activity as manifested by fever, sleeping pulse rate, electrocardiogram and sedimentation rate have returned to normal and the child is again alert, interested in his environment and gaining in weight. At that time a very gradual return to normal activity, under close supervision, should be instituted.

Coburn⁵ and Taran^{20, 21} have expressed the belief that massive doses of salicylates given early in the exudative phase change the course of the disease. This view has not been generally accepted. Murphy,¹³ in a histological study of the exudative lesions in patients with acute rheumatic fever receiving large doses of salicylates, found no evidence to support the contention that salicylates exert a specific effect on the underlying disease process. The value of salicylates in the symptomatic therapy of the exudative phase is universally recognized. Salicylate therapy should be discontinued for at least two weeks, with a reevaluation of the patient at the end of that time, before any other changes in therapy are made, for salicylates not only suppress the acute symptoms but alter laboratory findings.

The controversy over the use of digitalis continues. Pediatric cardiologists are extremely cautious in use of the drug. The toxic and the therapeutic dose are very close, and Taran²¹ has expressed the belief that, in active rheumatic fever, the toxic dose is less than the therapeutic dose. The drug may be of some value as a last resort in the patient with right-sided heart failure, but the results are not encouraging. The digitalizing dose is 100 mg. per 10 pounds of body weight, given in divided doses at intervals of six hours. The maintenance dose is 10 mg. per 10 pounds.

The dose of the more rapidly acting digitoxin is 0.1 mg. per 10 pounds of body weight, with a maintenance dose of 0.01 mg. per 10 pounds. Diginol® is given intramuscularly in a digitalizing dose of 20 to 60 mg. per 10 pounds of body weight, with a maintenance dose of 2 to 6 mg. per 10 pounds.

The mercurial diuretics have been recommended by Taran^{20, 21} for the treatment of congestive heart failure. The diuretic is given until a dry or stabilized weight is obtained, at which time the patient is put on a maintenance dose. This may be continued for months or years.

The use of continuous oxygen to promote cardiac rest and to reestablish the normal relation between systole and diastole has been urged by Taran.^{20, 21} This increases cardiac output and improves the general condition and well-being of the patient.

The indications for tonsillectomy for the child with rheumatic fever are no different than for the non-rheumatic child. If the tonsils are unduly large or diseased and the child is subject to recurrent otitis media, cervical adenitis and nasal obstruction, the tonsils and adenoids should be removed. The

operation should not be performed, however, until all signs of rheumatic activity have disappeared, since recrudescences may result from operation while the disease is active. Carious teeth or abscessed roots may be foci of infections and contribute to the continuation of the active phase of the disease. All infected teeth should be repaired during the inactive phase.

When any surgical or other procedures which might possibly spread a localized infection are contemplated a sulfonamide drug or penicillin should be given prophylactically preoperatively and for a week postoperatively.

SULFONAMIDES

The value of the sulfonamides in preventing recurrences of rheumatic fever has been amply demonstrated and reviewed by Hansen.⁷ It has been estimated that a child who is receiving a sulfonamide continuously is only one-tenth as liable to have recurrence as the child who is not. The dose is 1.0 gm. of sulfadiazine or sulfamerazine a day, and it should be continued for a minimum of five years, but preferably through puberty regardless of length of time. The patient should be examined for signs of intoxication at weekly intervals for the first six weeks and at six-week intervals thereafter.

Massell and co-workers¹¹ in a study of oral administration of penicillin in patients with rheumatic fever found that 100,000 to 200,000 units of penicillin three times a day completely eradicated hemolytic streptococci from the throats of 75 per cent. Even in those patients in whom the organisms were not completely eradicated, they were greatly suppressed so that streptococci were not shown on cultures during the period penicillin was administered. The authors felt that this indirect evidence indicated penicillin might be practicable for the prevention of hemolytic streptococci and hence for rheumatic fever prophylaxis.

Prompt sulfonamide therapy of streptococcal infections among rheumatic susceptible patients will not prevent rheumatic recurrences. Rantz and co-workers¹⁴ expressed the belief that prompt penicillin therapy of streptococcal infections interferes with the immune response by eliminating streptococci from the throat before toxins can be produced and disseminated in an appreciable quantity. It may be possible by prompt penicillin therapy of the streptococcal infection to prevent the chain of events which result in the rheumatic state.

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What's New in Pediatrics

Treatment of Erythroblastosis

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AFTER two years of trial of substitution transfusion of blood in the treatment of erythroblastosis, this method now can be better evaluated and earlier concepts revised. This presentation, then, will be concerned with the total experiences in Southern California with substitution transfusion, as well as with the mistakes that have been made and with suggestions for the safe and proper use of the procedure.

The substitution or exsanguination transfusion was originally developed in eastern centers in 1946 and 1947 and the first reports were glowing, as they usually are. In Southern California the first such transfusions were done in April 1947, and the poor results were alarming and confusing. There was at hand no set of indications for the procedure; mistakes were made and babies continued to die in spite of this new means of therapy.

For purposes of assay and appraisal, therefore, and to study the community effort rather than that of a specialized hematological center, records of all the cases of erythroblastosis in which substitution transfusion was used in a two-year period ending in April 1949 were gathered together. Comparisons between experience at Children's Hospital, Los Angeles, and that at other Southern California hospitals were made. For comparative purposes, data were gathered also on cases of erythroblastosis in which substitution transfusion had not been used.

Table 1 lists the data, which seem to indicate that substitution transfusion has not lowered the mortality rate in Southern California; in fact, it seems to have raised it. However, most of the cases in which substitution was used were severe, whereas most of those handled conservatively were mild.

In addition, the number of cases of cerebral damage that came to light was most alarming. About 15 per cent of the patients who lived turned out to be abnormal, either athetoid or simply slow in mental development. Similar experience has been reported in the literature. The cause of this brain damage is still unknown. Often the condition occurred in cases which were clinically mild. Most students of the disease feel that the damage takes place in utero and that no procedure will alter the development of this complication. It is interesting that these cases tended to be associated with very high maternal

TABLE 1.—*Mortality Rates from Erythroblastosis in Southern California*

	Number of Cases	Deaths	%
Cases in which substitution was used	45	13	29
Children's Hospital	16	4	25
Other hospitals	29	9	31
Cases in which substitution was not used: Children's Hospital....	35	5	14
Total Children's Hospital experience	51	9	18

antibody titre. Weiner's original thought that kernicterus was produced by the blocking antibodies and that hemolytic symptoms were produced by agglutinins is no longer tenable because agreement now is general that blocking antibodies are the only cause of all forms of hemolytic disease of the newborn.

Other positive and interesting findings included:

1. The history of a preceding sibling with erythroblastosis did not carry a particularly bad prognosis. This is contrary to the thought of Potter and others.

2. Erythroblastosis occurs most commonly in the second pregnancy.

3. Prenatal antibody titres had a definite correlation with the severity of the disease. However, the author disagrees with many of the workers in the field who state that a very high maternal titre invariably means a serious case with a high death rate. In ten cases in this series the titre was 1:256 or more, yet the patients lived and are well, half of them without having had substitution transfusion.

4. Substitution transfusions definitely cut down the length of hospital stay and the number of subsequent transfusions needed.

One relatively unpublicized procedure which has been most helpful has been the Coombs test, sometimes known as the developing test or the anti-globulin test. With this procedure used on the baby's cord blood it is possible to determine the presence of sensitized cells and the titre of any free maternal antibody, and thus get an idea of the probable severity of the disease—all before the baby may show any clinical evidence of erythroblastosis. Obviously such information is of value in determining whether or not to use substitution transfusion. Sturgeon, in a recent report on the use of the Coombs test, noted that the strength of reaction to the test was in close correlation with the severity of the disease, an observation which has been borne out in the author's

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TABLE 2.—Coombs Test Reaction Correlated with Severity of Disease

	No. Cases	Average (8.0 max.)	Died	Kernicterus
Severity				
Strong reaction.....	16	Severe (5.6)	5	0
Moderate reaction.....	23	Mod. (3.7)	2	2
Weak reaction	17	Weak (2.5)	0	1

experience (Table 2). Thus it is indicated that substitution transfusion should not be considered if the Coombs test reaction is weak.

In passing, the use of Rh hapten for treatment should be mentioned. This is an extract of Rh positive blood which was developed by Carter. It is lipid in nature and non-antigenic; it is said to specifically inhibit anti-Rh agglutinins and appears to be a hapten. The material was used throughout pregnancy in one very severe case and, in this instance, was of no value. The baby, which was born prematurely at seven and one-half months, was hydroptic and died a few minutes after birth. Sturgeon and Strong worked with this hapten serum two years ago and could not duplicate the results reported from the original work. Further work along the line of producing a neutralizing serum to be given the mother during pregnancy is certainly indicated.

Although many errors in technique have been made in use of substitution transfusion, the author feels that this "growing-up" period is now over and in the future the procedure can be used with relative safety and facility. So that others may not fall into error, the following list of dangers is presented.

1. In some cases not enough blood was given. For a baby of any size, at least 500 cc. is needed to supplement approximately 90 per cent of the original blood.

2. Transfusion was too long delayed. It should be done immediately after Coombs test results are known and the type of blood determined.

3. Blood was injected into the umbilical vein. In one case the umbilical vein ruptured, and in another thrombosis developed in the portal vein. The patients died.

4. Calcium was injected into the intravenous tubing. One patient died immediately afterward.

5. Protection of the infant against exposure, before, during and after the substitution, was omitted. Two infants had rectal temperature of 94° on admission to the hospital and two others had very low fluid intake for days before death.

The following plan of procedure eliminates the dangers listed and is relatively simple.

1. A set of indications should be established. (The author considers these factors as criteria: (1) maternal history indicative of erythroblastosis, (2) high maternal antibody titre, (3) baby born with evident disease or developing the disease in eight to 12 hours. Every decision is based upon the Coombs test reaction.)

2. Liaison with the obstetrician should be maintained so that titres are determined and transfusion can be undertaken without delay. In selected cases premature delivery may be indicated. The cord should be left long. It is probably best to clamp the cord early.

3. Helpful laboratory work on cord blood would be a cell count and smear for nucleated red cells, an icteric index, and a Coombs test.

4. The substitution should be as soon as possible.

5. The baby should be kept warm and in an oxygen tent from birth in severe cases.

6. The blood should be drawn out through the umbilicus, using the Diamond plastic catheter, and the substituted blood should be put in through the saphenous vein via a cutdown at the ankle. Two persons should do the substitution and the rate of injection should be exactly equal to the rate of withdrawal so that there is no chance of overloading the circulatory system. A 1:1,000 heparin solution in small amounts may be used to clean out the umbilical catheter if it becomes plugged.

7. Rh-negative, type specific blood should be used—at least 500 cc., and more if the maternal history indicates severe difficulty and the condition of the infant is poor.

8. Calcium is not really necessary. If it is given, it should never be injected into the tubing, but very slowly and directly into the vein.

9. After transfusion, the infant should be given fluids subcutaneously and kept in an oxygen tent.

10. Teamwork should be developed at the hospital among physicians called upon to treat erythroblastosis, so that one may be immediately available to assist the resident and to check on details.

Although substitution transfusion in the treatment of erythroblastosis has given disappointing results in Southern California thus far, technique is improving and ultimately a reduction in mortality rate may be achieved. It is noteworthy that in the last 12 cases (six quite severe) in which the procedure has been used, the patients have all gotten along well. Material for the Coombs test is now generally available to laboratories, and it is recommended that the test be used to assist in planning a course of action.

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What's New in Pediatrics

Paroxysmal Tachycardia in Infancy

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PAROXYSMAL tachycardia is rare in infants, although it is seen more frequently than it is recognized. It is important to the physician called upon to treat infants because it may be the cause of symptoms generally associated with a wide variety of other diseases, including diarrhea, pneumonia, and "idiopathic" cardiac enlargement. The symptom complex presented may lead to wrong diagnosis if the heart rate is not carefully counted. Paroxysmal tachycardia is important, too, as a possible cause of death, otherwise unexplainable, although it certainly does not underlie all or perhaps even the majority of unexplained and sudden deaths in infancy. Lastly, it is important because if the proper treatment is given, the response is uniformly satisfactory. Unless there is some associated and underlying disease which might of itself prove fatal, a situation which is not usual in such cases, treatment may well be life-saving.

In many instances the paroxysm will terminate spontaneously, without treatment, but as the condition is potentially dangerous, there is need for recognition and prompt treatment.

Review of the literature and solicitation of several hospitals and physicians in the Los Angeles area has yielded reports of about 100 cases of paroxysmal tachycardia in infancy. Less than 10 per cent of the patients had associated congenital heart disease. In almost 20 per cent of the cases the patient died, and although paroxysmal tachycardia with heart failure was not the true cause of death in all instances, still, some of these deaths might have been prevented.

DIAGNOSIS

As in many unusual conditions, diagnosis is based on a high index of suspicion and on careful examination, including accurate determination of the heart rate. Since infants cannot describe the palpitation that characterizes this condition in adults and directs attention toward the heart, the diagnosis is made from signs. The most common of these is failure to eat properly. Fretfulness and wakefulness may be noted, or the baby may be listless and drowsy. This may go on for several hours or days. Vomiting, or occasionally diarrhea, is present. Slight fever is usual, and leukocytosis is often noted.

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As the condition persists, signs of shock and of congestive heart failure appear, with dyspnea, tachypnea, cyanosis, hepatomegaly, cold clammy sweat, stupor, and, rarely, convulsions. The heart may be somewhat enlarged and there may be pulmonary congestion or pleural effusion. Auscultation will reveal very rapid heart action, often described as "too rapid to count," but careful study will permit accurate determination of the rate at least as fast as 250 per minute. It is rarely that the rate is slower than this in supraventricular tachycardia in infants, and in this respect it differs from paroxysmal tachycardia in adults, in whom the rate is usually between 150 and 250 beats per minute, often less than 200. Hubbard,¹ in 1943, reported one case of paroxysmal tachycardia in an infant with heart rate (proven electrocardiographically) of 353 per minute. The normal heart rate in infants is usually between 120 and 160. Sinus tachycardia at 200 beats per minute is not unusual, but paroxysmal tachycardia should be suspected if the rate is over 200 per minute and particularly if it is over 250 per minute.

Diagnosis is established by the electrocardiogram. This characteristically shows supraventricular tachycardia. Further definition as to auricular flutter or AV-nodal tachycardia is often impossible. Ventricular tachycardia is extremely rare in infancy, particularly in the first year of life. In the series reviewed it occurred in only five of 100 cases, and in four of these the diagnosis appeared questionable. If it is impossible to obtain an electrocardiogram to prove the diagnosis and the condition of the infant appears serious, it would seem reasonable and in the best interest of the patient to assume that a heart rate of 250 per minute or faster might be due to paroxysmal supraventricular tachycardia and to proceed with treatment based on this assumption.

TREATMENT

Digitalis is indicated. Many preparations are available, but it appears that lanatoside-C is the drug of choice. It is given intravenously (eliminating the uncertainties of absorption inherent in oral and subcutaneous administration), the dose can be accurately determined, and it has a wide margin of safety and is well tolerated.

No rigid criteria have been established for determining the proper dose, and various opinions have been expressed as to the tolerance and requirements of infants as compared to adults. A practical approach, and one that has proved satisfactory, approximates the application of Clark's rule, with

dosage based on the weight of the infant. One-hundredth milligram of the drug per pound of body weight may be given intravenously as the initial dose. After ten minutes each carotid sinus may be massaged. This is occasionally effective after lanatoside-C has been given, but not before. If the heart action has not become normal in 15 minutes, the same dose should be repeated. This is usually effective within 20 minutes. If paroxysmal tachycardia persists, one-half of this dose may be given after 30 minutes have elapsed, and may have to be repeated after another 30 minutes. Caution must be used not to overwhelm the infant with too much of this potent drug, lest the treatment itself prove fatal.

Rarely, lanatoside-C may not be effective, and in this unusual situation more dangerous drugs should be considered. In one such case, ouabain proved life-saving. The dose of this drug may also be calculated according to Clark's rule. Various other drugs have been tried, and there are several reports of the successful use of mecholyl, but the administration in each instance appears to have precipitated alarming and hazardous reactions, and even death.

L. T. Bullock, M.D., and H. Rollman, M.D., gave the author permission to summarize, for this presentation, certain data which will appear in greater detail in a forthcoming article, which will include a complete bibliography.

PROPHYLAXIS

Once an attack has been terminated, the question of prophylaxis must be settled. Frequently there is no recurrence, and no prophylaxis is needed. Sometimes recurrences are so widely spaced that the value of prophylactic drug administration is questionable as it may seem more satisfactory to treat each attack on appearance. If the arrhythmia appears twice within a week or less, however, prophylactic administration of some potent digitalis preparation appears warranted, with the objective of maintaining full digitalization. The daily maintenance dose is approximately 10 per cent of the digitalizing dose. Daily administration of 20 mg., or slightly more, of digitalis leaf or its equivalent of tincture of digitalis is usually satisfactory. The same precautions regarding possible toxic effects are required in treating infants as in older individuals, and constant supervision is essential. Once prophylaxis is started it should be continued for at least a month and perhaps longer.

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Fractures and Dislocations of the Carpus

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SUMMARY

Although one-eighth to one-tenth of all fractures of the wrist are carpal fractures, they may be overlooked, unless attention is directed particularly to them in diagnostic examination. Symptoms may be slight or lacking, but diagnosis is important because such injuries may give rise to pain or disability later. There are certain guides and procedures in physical and roentgenographic examination which make diagnosis easier and more certain. Treatment depends upon the nature of the lesion. It must be based on all the knowledge obtainable by examination, mental review of the anatomy and pathologic changes, inquiry into the cause of injury, and the interpretation of roentgenologic findings.

In all classes of civil, industrial and military medical service involving injuries, perhaps less is known by the average physician about carpal fractures than other skeletal injuries.

Although most if not all physicians would agree that their knowledge of and treatment for the common fracture of the lower end of the radius, the most frequently encountered injury near the wrist and the first cousin of carpal fractures, was satisfactory from all standpoints, their knowledge of carpal injuries is small. Clean-cut interpretation of these carpal injuries by the roentgenologist and the adoption of a workable standard of description or clinical classification have lagged behind the rate of their occurrence. Physicians now meeting these injuries daily in their work believe they are entering new fields; in reality they are merely observing their patients more closely and are being forced to understand definitely why apparently small and often unrecognized injuries lead to prolonged and painful disability.

Men working in machine shops and factories, struggling with artillery in the field and on the road, or employed in airplane service have undergone a large number of carpal injuries. Meekinson in a year's service in the Air Force encountered about 110 fractures of the navicular as enumerated in his report of June 1, 1944. Colonel L. H. McKim, as consulting surgeon of the Canadian Army, in two years encountered 125 navicular fractures, all of which healed without a single instance of nonunion. Other observers have reported smaller groups here

and there; the aggregate is quite large. The proportion of these injuries will be maintained for a long time, and fortunately alert physicians and roentgenologists will now recognize them early and in so doing will treat them successfully.

ANATOMICAL CONSIDERATIONS

The anatomy of the bones, their encasing ligaments, their articular surfaces and synovial coverings, their range of movements and their all-important blood supply must be understood by the physician. Without this knowledge he cannot interpret the roentgenogram of acute or progressing lesions, the ancient or healing lesion. He cannot define the fracture or accompanying dislocation, and he consequently may be unable to apply the best line of treatment.

Clinically and anatomically the carpal bones are divided into two principal rows or groups. The proximal row contains the os naviculare, os lunatum and os triquetrum. The distal row comprises the os hamatum, os capitatum, os multangulum majus and minus and the os pisiforme. The radiocarpal joint is condyloid. Entering into this joint are the lower end of the radius, the distal surface of the triangular disk and the carpal navicular, lunate and triangular bones which fit into the elliptical and concave surface of the forearm element. The articular surfaces of all these bones are covered with cartilage and the joints are surrounded by strong capsular ligaments strengthened by interlacing dorsal and volar radiocarpal, intercarpal and two lateral ligaments, the radial and ulnar collateral ligaments. Flexor and extensor tendons crossing the carpus, bound by the annular ligaments of the wrist, further strengthen and protect the carpal joints to maintain a powerful attachment of the hand to the forearm.

The blood supply comes through the attachments of these ligaments of the carpal bones from small terminal volar and dorsal branches of the ulnar and radial arteries and the metacarpal vessels. Blood vessels do not enter the bones on the articular or smooth cartilaginous surfaces. The blood supply is consequently scant and not uniform and may vary with individuals or the different bones. The navicular has a natural wide variation of its blood supply, both in location and quantity, which may enter as a factor in healing or necrosis after fracture or injury.

Most radiocarpal motion occurs between the radius and proximal row of carpal bones both in the volar-dorsal axis and in the lateral motion. There is much less motion between the two rows of carpal bones at the mid-carpal joint and still less at the distal margin or carpometacarpal joint.

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INCIDENCE

About one-eighth to one-tenth of all fractures of the wrist, including Colles' fracture, are carpal fractures. In order of occurrence the injuries of the carpal bones are: Fractures of the navicular in various parts of its body, dislocations of or around the lunate bone, fractures of the lunate, fractures of the navicular plus dislocations, injuries of the triquetrum, and complicated fracture dislocations involving the proximal row and the midcarpal and radiocarpal joints. Isolated fractures or dislocations of or around the bones of the distal row are quite rare but must be looked for after hand and wrist injury.

ETIOLOGY

The cause of a carpal fracture is usually a fall on the outstretched hand such as causes Colles' fracture. In the face of definite fracture of the radius and demonstration of it by roentgenogram, the surgeon may very easily overlook an accompanying injury of the carpal bones. This is particularly so because the first film made soon after the accident may not show a definite plane or line of fracture across the injured carpal bone, as has been observed in many injuries of the navicular. The cause may be a minor blow or even a twist of the wrist, under pressure or strain; it may be forgotten by the patient. Later symptoms and findings bring out the pain and disability of real bone injury, and the roentgenogram finally shows the fracture plane or the resulting change of density of fragments or aseptic necrosis, usually resulting from interference with blood supply and enforced use or lack of rest and splintage.

Suspected injuries of the carpus must consequently receive careful and complete physical and x-ray examination at the time of injury. In event of real complaint of pain or local tenderness, the wrist may profitably be put at rest on a splint with the hand in neutral position, followed by reexamination after one or two weeks by roentgenogram for delayed-appearing planes of fracture, even when no primary separation of fragments is found. Evidence of necrosis of parts of the bone involved resulting from changed vascular supply, as betrayed by changes in density compared to neighboring bones, must be searched for in the roentgenogram. The navicular is the worst offender in this class of injury, because it is the most often injured carpal bone, because it has the greatest range of movement in the carpus, because its blood supply is the most variable and because on account of its anatomical situation it is subject to the greatest strain and compressions. Direct violence from blows on the wrist may likewise cause these injuries, often without open wounds.

Violence of a fall or blow on the wrist may lead to a mere crack across the bone involved—most often the navicular—with resulting pain which may interfere with functional use of the hand and yet may entail, immediately afterward, no evidence of displacement of fragments, comminution or compression, or, most unfortunately, even the finest

plane of fracture in the roentgenogram. Sometimes this plane is so faint, so indefinite, that it is considered by both roentgenologist and the examining physician as a normal marking of the bone and is, at least temporarily, not recognized for its true worth. Compression or twist violence or fall may not cause separation of fragments. These often interfere with the continuity of the bone surface; both cortical and internal cancellous bone may be cut off from precarious blood supply, resulting in local aseptic necrosis, slight bone absorption and ultimate appearance of a fracture line or plane seven to 14 days later. When separation, impaction or comminution are caused at the time of fracture, roentgenologic recognition is not difficult and the fracture then is seldom overlooked.

These descriptions apply mainly to the navicular; they may apply to any of the proximal row of bones; they may even apply to the distal row of bones, and the condition may develop there very slowly. The lunate often suffers compressions, early unrecognized, only to undergo late aseptic necrosis with increased bone density as compared to surrounding bones seen in the roentgenogram. The day or incident of the causative trauma may be forgotten. A physician may be able to determine how old such a condition may be from the depth of the increased density of the bone, from the reaction of surrounding bones displayed by new bone formation or natural effort at fixation of the intercarpal joints by osseous outgrowth, or by shrinkage and collapse of the individual bone and the reaction of the wrist by pain, fixation and atrophy of soft structures. The injured person may then be entitled to consideration of injury forgotten or overlooked both by himself and his physician.

From a pathologic standpoint, fractures of the navicular may be divided into several groups. The first classification is recent or ancient fracture. The second is whether the lesion is fracture of the tubercle, ordinary transverse fracture, usually seen near the center of the bone, comminuted fracture which may involve the whole body or simply one of the fragments of it, proximal or distal to a transverse dividing plane through the bone. Impacted fracture, usually through the body of the bone, is still another type. This results in impaction of the distal fragment into the proximal along a rough irregular plane with some axial deviation of the distal portion and longitudinal splitting of the bone, which is very rare. Some transverse fractures are near the proximal end of the bone and lead to early necrosis of the proximal fragment, which is thus quite completely cut off from arterial blood supply via the small nutrient arteries and devoid of periosteal blood supply because the fragment lies almost completely free from ligamentous attachment as a loose intra-articular portion.

Dislocations. Pure dislocations which almost always involve the lunate, or the fracture-dislocations which may involve the proximal half of the navicular and all the lunate, are difficult to read in the

roentgenogram. These two pieces may be dislocated out of the radiocarpal joint or retained there. If retained in normal relationship with the distal articular surface of the radius, there may be accompanying dislocation of all the rest of the hand and carpus around the two portions mentioned either dorsally onto the top of the wrist or in volar direction. They may cause great pain, swelling, stiffness and gross loss of function of the hand and immediate complications from nerve involvement (median). There is local hemorrhage, tearing of ligaments and finally extensive bone necrosis from interference with circulation unless reduction is made or misplaced bone is removed to permit normal blood flow over intact avenues.

DIAGNOSIS

The symptoms of carpal fracture may be very slight or lacking. An injured individual may never report for professional examination, unless working under control and ordered to do so, even for sprained wrists. Physical examination should be painstaking and thorough, with both arms fully bared for viewing and comparison of range of motion in the wrist joint. The patient should sit with hands comfortably outstretched on a clean surface. The range of wrist motions, *without movements of the forearm, arm or shoulders*, should be tested and compared in all directions. Local tenderness over the proximal row of carpal bones, and then over the distal, should be searched for. The anatomical snuff-box should be tested by the tip of the examiner's index finger or the dull end of a pencil with the patient's thumb held outstretched. Tenderness here leads to suspicion of navicular injury. All swelling, over-thickness, lessened range of motion in the wrist and numbness in the fingers, especially in the median distribution, should be noted and recorded. The examination should be gentle. All findings should be recorded in writing.

Roentgenographic Diagnosis. A roentgenogram should be made in at least two planes with the center ray directly over the radiocarpal joint. The lateral view should show the forearm so that the shadows of the two forearm bones overlap exactly, thus giving a clear shadow study of the usual relationship between capitate, navicular and lunate in the carpus. If any other bone than the navicular is suspected of injury, additional oblique films may be required to throw the shadow of the bone suspected of injury out into clear profile view. The physician should not be satisfied with any film which does not give clear definition of the suspect area. The film should be studied carefully and methodically. It takes much practice to learn to read carpal films.

Even if a fracture plane in the navicular (most common injury) is not seen, if no dislocation of carpal elements is found, the patient should not be dismissed too easily. Support should be applied and the patient told to return in a week or ten days for another film. This must always be done if any pain or disability persists and is the best plan for all patients in the long run.

TREATMENT

Treatment of carpal injuries must be based on all the knowledge obtainable by the examination, a mental review of the anatomy and pathologic changes, an inquiry into the exact cause and nature of the injury and an interpretation of the roentgenologic findings.

Treatment of Open Wounds. Immediate treatment after diagnosis of fracture or fracture-dislocation depends on the nature of the lesion. If an open wound exists, it must be surgically cleansed and débrided, even if it is but skin deep. If there is a deeper laceration with joints opened into and possible nerve or blood vessel injury, the surgical care becomes a major procedure. It should not be attempted in any other surroundings than a properly prepared operating room. To minimize loss of tissue, unnecessary extension of wounds, loss of blood and in-carrying of additional infection from unwise sponging or manipulation, and to render the repair as anatomically perfect as possible, the operation must be performed under general anesthesia and with the use of a constrictor on the arm to ensure a bloodless field. During the repair of soft parts injury and exposure of the carpal joints and bones, a complete reduction of the fracture, its fixation if required, or a reduction of the fracture-dislocation under direct vision in an open wound may be possible. This may entail the use of strong traction (by assistants) on fingers or hand, counter-traction on the forearm, and manipulation. If instrumental aid is required to assist in open reduction of displaced fragments, this help must be of the most gentle character to avoid injury of the cartilaginous joint surface of any bones and also to avoid further jeopardy to the already interfered-with blood supply by tearing or stretching of ligaments. The highest degree of preparation of an aseptic field and maintenance of aseptic technique in the operation must be obtained. After reduction, the use of antibiotic drugs may be indicated as in any open wounds or fracture, according to the nature of the wound, its soiling or the surgeon's practice. Hemostasis must be secured by minimal ligation, nerves should be approximated and sutured if possible, and severed tendons may be identified but not always primarily sutured, depending on the surgeon's ability and the nature of the soiled wound.

Dressing and Splinting. The wound is dressed, either with loose vaseline gauze pack or as a finished closed débridement. The hand, wrist and forearm are splinted with moulded plaster of paris strips laid on dorsal and volar surface, over adequate wound dressings, in a neutral position or one demanded to maintain reduction by the character of the fracture or fracture-dislocation. Wound dressing is performed as infrequently as possible. Each dressing may require removal of splintage, in which case there must be adequate help to hold the hand and forearm in quiet position. If the wound remains aseptic, the length of time for immobilization will

equal or exceed by 50 per cent that required for the healing of the ordinary closed lesion.

If there is no open wound and no fracture or fracture-dislocation verified by the examination and the roentgenogram, but there is evidence of local tenderness, interference with function and complaint of pain, the hand and wrist must be immobilized either on a padded splint or in a moulded plaster of paris splint. If injury of the navicular is suspected, the splint must extend from the metacarpophalangeal joint to just below the elbow with the hand in a straight position. The thumb should be partly abducted, fully extended and immobilized nearly to the tip, which may be left exposed so that the circulation may be observed. After seven to ten days a second roentgenogram may be made through the plaster. Developing planes of absorption or definite fracture often appear plainly through the encasing splint. If they are found, the splint, not having been removed, does not have to be replaced, thus gaining the advantage of not moving the fragments after their first fixation in the plaster. The time elapsed since the injury was first splinted can then be added to the total number of days required for complete immobilization of the wrist.

Fracture of the Navicular. For fracture of the navicular, a closed and isolated injury, immobilization in plaster of paris must be employed as soon as a diagnosis is made.

Fracture of the tubercle with adequate natural blood supply usually heals rapidly in two to four weeks, without definite immobilization but with restriction in use. During the healing period roentgenologic control is used to show proof of bony union and to confirm full use of the hand.

Whichever type of fracture of the body of the bone may be present, it is doubtful that local pressure or manipulation may change the angle or approximate the surfaces more evenly unless a dislocation exists. If fragments are dislocated as in fracture-dislocation, a manipulative effort under anesthesia is indicated to restore approximation. Any rough manipulation or undue pressure may add to interference with local circulation and increase the time required to restore it and to establish bony union in the bone. Consequently the hand and forearm are gently cleansed, washed with alcohol, covered with stockinet (including thumb in added small stockinet cover) and held in neutral position by a reasonably heavy plaster of paris circular dressing from the elbow to finger bases. A sling may be used during the first few days after splinting until the plaster has hardened and any edema in the hand is absorbed. The author finds it advantageous to pad the ulnar styloid with a small piece of felt to avoid painful pressure later. A quite heavy plaster is indicated because the patient may return at once to work or other activity and not carry the forearm in a sling, but may use and move the arm and fingers where free, thus avoiding muscular atrophy and diminished circulation in the arm as a whole. Likewise the arm thus used is subject to

innumerable jolts and blows daily which may indent or break the plaster and lead to replacement long before the surgeon wishes to remove it or x-ray the bone for progress in healing.

For young vigorous adults and adolescents this dressing must remain undisturbed from six to ten weeks if it can be made to wear that long. To remove the plaster encasement, it is cut along the radial side and out along the thumb portion so that it may be spread and slipped off *without moving the wrist*. Immediate roentgenogram is then made to inquire into the amount of bone healing. When bone healing is quick the fracture plane as such may be obliterated in six to ten weeks. The hiatus, if any, at the site of fracture will be filled with calcified osteoid tissue. In six or ten weeks this will probably not be mature and organized into well-defined bony trabeculae similar to the markings found in the body of the bone, but it may represent a clinical union on its way to maturity provided the wrist is not mistreated by overuse. If such a condition of plastic union is found, the splint may be left off, the patient advised to start use very gradually and gently and to spend time massaging finger joints, exercising the hand by squeezing a suitably sized ball, but not by forcing wrist motion. The author is of the opinion that too hot applications or soaking of the hand and wrist are contraindicated in the further rebuilding and maturing of this still untrabecularized bone. Gentle, steady, active use by the patient—nothing forced or strongly manipulative—is indicated. Within a month a second roentgenogram should show further maturity of the bone, any local soreness should have disappeared and the function of the wrist and hand should be much improved. If this is not found and there is evidence of absorption of osteoid tissue about the fracture plane or planes, the hand and wrist should again be immobilized as before. It is far better to give an apparently too long immobilization than a too short one.

If, after the removal of the plaster as outlined, the fracture appears not united, a circular plaster of paris dressing should be reapplied at once, without movement or any manipulation of the wrist. The dressing should be worn an additional period of six weeks and the fracture site reinvestigated by x-ray. Several such plaster dressings may be needed to obtain a final bony union, proven by x-ray examination and verified by painless increasing range of motion and functional use. Some patients require as long as 10 to 14 months of such treatment.

Dislocation. If fracture-dislocation is present, is diagnosed, is understood in the displacement of its various components, the surgeon must make every effort, in the case of recent injury, to effect manipulative reduction. This can only be obtained under full anesthesia and with sufficient assistance, especially in the case of manual laborers who have powerful wrists and forearms. The patient is rendered completely lax by the anesthesia. The shoulder of the affected arm is partially abducted and the

arm is held by an assistant in that position, grasping firmly with both hands, with his feet well planted on non-skidding floor, as far out of the operator's way as possible. Two assistants may be helpful—one on the opposite side of the table from the operator.

Depending on the type of dislocation, whether dorsal or volar, the operator then plans the manipulation. The first step is a *prolonged traction on the hand*, while assistants make the counter-traction. Traction is maintained in the direction opposite that of the dislocation: For example, in volar dislocation of capitate and other distal row bones, the pull is slightly upward and in full extension. This must be kept up several minutes and during the course of traction the bones may be felt sliding into place. If this is not successful at first, it must be repeated and can be helped by the pressure from the thumbs of an assistant against the overriding bulging mass of bone at the dislocation site on whichever side of the carpus the bulge exists. Prolonged effort and much strength, smoothly and persistently applied along with deep anesthesia, will usually effect reduction, after which an x-ray film is made at once and the forearm, wrist and hand put in a plaster dressing as described for simple fracture. Some care has to be taken of the amount of swelling; the radial pulse must be certified; the sensation and movement of the fingers checked and the condition recorded in writing as soon as anesthesia passes off. The length of time of immobilization must be gauged by the fracture more than the dislocation. Bony union must be obtained before use and movement are started; if not, the result may be a reduced dislocation but an ununited bone.

If manipulative reduction does not succeed under anesthesia, it is best to desist for the time, to cleanse hand and wrist and encase in a sterile dressing or towel, elevating the hand on a pillow for a short time. If no bullae appear, another x-ray check may be permitted and plans for operative reduction or excision of bone fragments planned. The physician should not be in too much of a hurry, for he must make sure the skin is clean and can be rendered aseptic for what may prove to be a long and difficult operation.

The navicular and lunate take the longest time to heal after fracture-dislocation. The author has observed earlier and successful unions in the triquetrum—eight weeks in two cases. The pisiform often takes ten weeks.

ANCIENT FRACTURES

Diagnosis. Ancient fracture may be diagnosed when the patient is seen late—several weeks after injury—when there have been inadequate efforts at immobilization or none at all, or when the injury has been called a sprain or has been unrecognized, or when the patient has not previously consulted a physician. The symptoms of pain, local tenderness, restricted wrist motion, slight deformity and functional interference persist in a varying degree—some not unpleasantly, others in great intensity.

There may be evidence of nerve injury, especially the median or its branches. The roentgenogram shows a spreading area of necrosis around the fracture plane, cystic absorption of much of the body of the bone (especially the navicular) or fragmentation, increased density as compared to its neighboring bones, and sometimes new bone formation extending from adjacent bones into the joint areas about the fractured bone. Some patients appear five to ten years after fracture with pronounced cystic changes in the interior of the bone and increased density of the partially dead and partially healed cortex.

Treatment. Some ancient fractures, even with the advanced pathologic changes suggested, may yield to prolonged immobilization as described. The fracture dislocations will not thus yield because much of the functional disability in them is mechanical, as in an unreduced dislocation at any joint. In such cases, well planned excision of bone is required, freeing enough space to permit some hope of recurring motion when the muscles moving the joints become reeducated. Such excision of bone should attempt to stick to old joint lines and leave intact cartilage behind. For instance in a transnavicular perilunar dislocation, ancient and unreduced, the indication would be to perform a carpallectomy—a removal of at least two of the proximal row carpal bones, namely lunate and navicular, including the navicular fragment adherent to the distal displaced row, and closure of the wrist with subsequent early motion and muscle training. This operation must be done without adding any injury to bones, cartilaginous surfaces of adjacent joint, nerves and tendons in the area opened. It can only be done under general anesthesia, under a constrictor, with suitable instruments and adequate anatomical knowledge of just what structures are being excised. In some instances the triquetrum must also be excised along with the other two bones. The capitate then retracts to the articular surface of the radius, a new joint motion is obtained between capitate and radius, and a reasonable functional return is achieved, with an almost undetectable shortening of the carpus. Careful planning of the amount of postoperative splinting, starting of motion and massage must be done in each case.

For the uncomplicated ancient fracture (as of the navicular alone) surgeons must have some operative attack when prolonged immobilization is refused or is objectionable from any standpoint. Such methods are: (1) Complete excision of the offending ununited bone, leaving a hiatus in its place or inserting a replica of vitallium or other metal in the defect; (2) attempts to overcome the nonunion by (a) drilling across the fracture plane, (b) insertion of one or more small bone transplants. In cases of long standing in which the surgeon cannot be sure whether or not dislocation may have been a complication, fusion of the radiocarpal joint may be the procedure to relieve pain, to strengthen the joint and ultimately to increase the functional use even in the face of the permanently stiffened articulation.

Complete excision of the offending bone is frequently done for irreducible dislocations of the lunate, some of which may not be so ancient. The carpus seems to get along quite well without this bone. Incision is made on either dorsal or volar surface of the wrist under anesthesia and constrictor, and no structures in the wrist should be damaged. All tendons, nerves, etc., should be gently retracted. The annular ligament may be cut but must be resutured and the articular surfaces of the remaining bones must not be damaged. Tight closure and little if any splinting are required after this relatively simple excision of the lunate alone.

Excision of the proximal row is much more difficult, especially when it is necessary to find and bring out the distal fragment of the fractured navicular, which clings to the distal row. It is an operation of major difficulty and the instructions given for all such operations must be followed.

For excision and fusion of the radiocarpal joint the author prefers an approach on the ulnar side of the wrist, partial excision of the lower end of the ulna and a block of bone thus obtained tucked into the area to be fused. This is followed by prolonged plaster of paris splinting.

Ancient or ununited fractures of bones—the navicular, as an example—which are to be left in place and cared for by operation may be treated by drilling through a small opening in the "anatomical snuffbox" at the base of the thumb, using x-ray control at the operating table to be sure of the direction and extent of insertion of the drill. Long immobilization in plaster is required with the same criteria for establishing union as after nonoperative treatment. This method has been used successfully many

times by the author; it is simple and apparently highly efficient.

Bone Transplants. Bone transplants have also been used to obtain union in ununited carpal bones (navicular). The transplant may be inserted in a prepared bed in the bone after dorsal exposure, or it may be inserted through drill holes made via the snuffbox. The first-named method is a little grosser and may interfere further with the blood supply of the bone. Via the snuffbox the operation is delicate, but quite sure, and no interference with the vascular supply of the navicular need follow. Both methods require the usual subsequent prolonged immobilization. Functional results may not be forthcoming for one or two years after operation and then may not be up to the patient's expectation, yet pain and other symptoms may be absent.

Metallic Insertions. Recently Waugh made some vitallium replicas of the carpal navicular to be inserted in the site of ancient fractures after removal of the fractured navicular bone. As yet, few such substitutions have been done in man. It may offer a quick way out for the comminuted fracture, for the complicated fracture-dislocation, and the non-united or ancient fracture with or without cavitation in the bone. The author believes that, with the small amount of range of motion in the radiocarpal joint, no analogy can be drawn as between this operation and the result following the insertion of a vitallium cap on the head of the femur in the wide normal excursion of the hip joint. The author has examined some of the patients thus operated upon. In most cases there was restricted motion but not much pain.

122 South Michigan Avenue.

Cancer Detection Centers

The Experience to Date in California

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SUMMARY

Cancer "detection centers" (that is, centers for the examination of presumably well or asymptomatic persons) have been tried out in four different California communities during the last three years. In all instances—as in most other such centers throughout the United States—they have not been successful in restricting examination to well persons.

The detection centers in California may therefore be described more accurately as "cancer examination and detection clinics."

Three of the four centers have been closed owing to the small yield of cancer cases discovered, plus the fact that the cost of operation exceeded the total available funds of the local branch of the Cancer Society. In addition, it was extremely difficult to obtain and maintain competence on the part of the professional staff in such centers.

A more practical approach to the problem of earlier tumor detection would appear to be emphasis on making "every physician's office a detection center," and stressing the annual examination of persons over 40 years of age for tumors in the five common accessible sites. These are the tumors most readily curable today.

EARLY in 1946 the Cancer Commission of the California Medical Association decided to support the trial of a few medically sponsored and supervised cancer detection centers to be located in different areas of the state. To that end, it drafted a set of minimum standards for such centers, and the standards were approved by the Council and House of Delegates of the State Medical Association on May 9, 1946.

Four pilot centers were developed by local county groups and had operated for from 17 to 25 months at the time of the preparation of this report. They were located in Santa Barbara, Fresno, San Francisco, and Ventura. Three of them have now closed. The experience with all four to date constitutes the basis of this report.

This report has been submitted to, and approved by, L. C. Kinney, M.D., Chairman, and Frederick Hook, M.D., Medical Director, the Cancer Commission of the California Medical Association. The author is a member of the Cancer Commission.

Read before the National Conference on Cancer Detection, sponsored by the American Cancer Society, Portsmouth, New Hampshire, September 9-11, 1949.

TERMINOLOGY

Initially, the term "Detection Clinic" was used, but, since "clinic" implies to many persons a place wherein the sick are diagnosed and treated, and since detection agencies were designed for the examination of apparently well persons, the term center was soon substituted. This, of course, did not eliminate confusion; it merely reduced it.

To aid in clarifying the functions of the various cancer-fighting agencies of the medical profession and the American Cancer Society, the following terms were developed and have been used in the state:

1. *Cancer Information Center.* This center is a county branch office of the state division of the American Cancer Society, which attempts to furnish information to inquirers on matters pertaining to cancer prevention, diagnosis, or treatment. As a general rule, the center refers patients or examinees to physicians chosen in rotation from a panel furnished by the local county medical society, or, in the case of indigents, to a suitable free clinic as near their residence as possible. While detection centers were being tested, a certain number of applicants were referred directly to them.

2. *Cancer Detection Center.* This was a pilot center to which it was planned to direct for examination only those persons who had no signs or symptoms of tumor. It was operated by local agencies, with the approval of the local county medical society, and the support of the local branch of the Cancer Society. Funds of the latter were augmented by a nominal payment by some examinees, and by money from other sources such as the State Division of the American Cancer Society.

3. *Consultative Tumor Board.* This is a volunteer board composed of physicians and surgeons interested or qualified in cancer work (especially pathologists, surgeons, and radiologists), which meets periodically in a given hospital or other medical institution, and offers advisory recommendations as to diagnostic or therapeutic procedures on patients referred by other physicians. It provides consultation on adequately worked-up cases.

4. *Treating Physicians and Surgeons.* These are radiologists, surgeons, and other physicians to whom patients are referred for treatment.

In the above list of agencies the terms "clinic" and "facility" are carefully avoided. Some "cancer clinics" furnish only simple physical examination; others furnish complete diagnostic studies; a few provide complete diagnostic and therapeutic serv-

ices. Some are for indigents only; others accept only pay patients. It cannot always be determined from a distance which function a given "cancer clinic" fulfills. Therefore, until such time as there is clarity regarding the services actually available, it may be best to defer using the word. For the same reason "facility" is eschewed. A building may contain microscopes, stains, and technicians, but without a competent tissue pathologist it is of little value to the public or profession as a cancer diagnostic agency. Similarly, an x-ray unit or a few capsules of radium (both of which are often referred to as therapeutic facilities) are worthless without an accompanying physician trained in their usage.

MINIMUM STANDARDS—THEORY

The work of the early detection center advocates led to the following definition being adopted by the American Cancer Society and approved by the American Medical Association:

"The cancer detection, cancer prevention or well-person clinic is designed to detect abnormalities not producing symptoms sufficient to send the patient to the doctor. These clinics do not diagnose or treat diseases."

In order to underline this aspect, the following Statement of Purpose was issued in 1946 by the California Cancer Commission:

"The purpose of the 'detection clinic' shall be to make periodic physical examinations of presumably well persons to discover early chronic disease with special emphasis on the early recognition of cancer or lesions that may lead to cancer."

The Minimum Standards for Detection Centers adopted by the California Medical Association in May 1946 are:

"1. The 'detection clinic' shall have the continued approval and support of the county medical society. The clinicians must be members of that society.

"2. The clinic must be conducted in the outpatient department of a Class A medical school or an approved hospital. If located away from the institution, it must be operated as an integral outpatient department of that institution.

"3. Where there is no approved hospital or medical school in the community, the 'detection clinic' will be operated by the county medical society and all of the activities will be under the immediate supervision and control of the society. The clinic shall be conducted in a local hospital unless special approval is granted by the Cancer Commission after careful investigation.

"4. The clinic shall be supervised by a physician who has had training and experience in the diagnosis and treatment of cancer.

"5. The clinic shall have proper housing and adequate facilities and supplies to conduct complete physical examinations. The clinical laboratory and x-ray departments shall be easily accessible to it.

"6. A sufficient number of clinicians shall be available to conduct the clinic at regular intervals and to provide for complete physical examination of every patient accepted by the clinic.

"7. Adequate records shall be kept of the history, physical findings and recommendations, and of the disposition of patients. Sufficient personnel shall be available to provide for necessary nursing, stenographic and record services.

"8. The examination shall include: (a) history; (b) routine blood count, urinalysis and serology; (c) x-ray film of the chest (mass survey); (d) nose and throat examination, including lips and intra-oral; (e) examination of the breasts; (f) physical examination of the chest, abdomen and extremities (including skin); (g) examination of lymph nodes: neck, axillae and groins; (h) pelvic examination; (i) rectal examination; (j) Papanicolaou vaginal smear (where feasible).

"9. Examinees that present suspicious history or abnormal physical findings shall be referred to their family physician for diagnosis and treatment. If there is no family physician, the patient shall be referred to a physician or clinic as directed by the policy of the county medical society.

"10. A summary of the pertinent facts and recommendations of the clinic shall be sent to the physician or clinic to whom the patient is referred.

"11. One month after such reference to physician the case shall be followed up by letter or social service visit and a complete report of the diagnosis and treatment shall be obtained.

"12. Only presumably well adult patients will be accepted for examination. No patient under treatment for cancer will be accepted without permission of the attending physician.

"13. Examinees shall be expected to make uniform contributions toward the expenses of the clinic if able to do so, but this shall not be in excess of the established cost of the examination.

"14. All publicity concerning the clinic must have the approval of the county medical society.

"15. Regularly scheduled periodic meetings will be held by the staff to study, review and follow up the cases seen in the clinic. An annual report of the work of the clinic will be sent to the Cancer Commission."

MINIMUM STANDARDS—PRACTICE

In practice, it was soon found impossible to limit examinations to presumably well persons. For one thing, local physicians sometimes thought the center was a free diagnostic clinic and referred deserving symptomatic persons for study and the social service worker or attending nurse was loath to turn them away. For another, persons who had been given a diagnosis of cancer elsewhere came in saying that they "felt quite well but wished a check-up." When the sincere and hard-working physician (who had often just examined a score of persons without evidence of cancer) triumphantly found a stony hard prostate (and a chest x-ray was reported as showing metastases), the patient merely remarked, "Well, I wanted to be sure that those university hospital doctors were right!" Such examples are not exceptional.

In none of the four "pilot" detection centers,

therefore, were examinations confined to presumably well persons without symptoms. It was impossible to do so. The following figures accordingly represent the results of examination of a miscellaneous group of persons, symptomatic, follow-up and otherwise:

In the four centers, 2,479 persons—342 males and 2,137 females—were examined between October 1946 and August 1949.

From the data available, it is estimated that not more than five cases of cancer were detected in persons without symptoms. All of the other cancers detected were in persons with frank tumors in the lip or breast (who came for advice), or in persons with symptoms such as bloody vaginal or rectal discharge, who presented themselves for free or part-pay diagnosis and treatment.

Including these persons with symptoms and some who had obvious recurrences and were seeking follow-up examination, a total of 40 proven cancers was reported.

In Center A, 748 persons were examined during a period of 25 months; 25 cancers were observed.

In Center B, 930 persons (females only) were examined during a period of 24 months; 7 cancers were observed. (Skin 2, nasal cavity 1, breast 2, cervix 2.)

In Center C, 376 persons were examined during a period of 17 months; 8 cancers were recorded. (Lip 2, breast 3, cervix 2, sigmoid colon 1.)

In Center D, 425 persons were examined during a period of 18 months; 14 were suspected of cancer; 11 of these are now under observation and one is scheduled for operation.

Of the entire group of 40 persons with established cancers, 38 have been given some form of surgical or radiological treatment, and in a majority of these cases, the cancer is recorded as arrested at present.

OTHER FINDINGS

In addition to cancers, other lesions were, of course, discovered. Some of these were justifiably labeled precancerous and the finding of them represents a worthwhile yield. However, the term precancerous is not calculated to diminish cancerophobia in the susceptible, and should be used with greater discretion than was shown by one center which listed as precancerous the following entities: 1. Verruca; 2. Pigmented nevus, axilla; 3. Fibromyoma uteri; 4. Suspicious smear. The psychologic damage resulting from casual use of the term precancerous, or from giving a false positive diagnosis of cancer, is not to be lightly regarded.

Some persons were found to have ailments such as hypertension, emphysema, arthritis, and so forth, which resulted in referral to physicians and, presumably, in benefit to the examinees. Space does not warrant a complete listing of these findings herewith.

DISCUSSION

The concept of the detection center for apparently well persons is understandable and logical. How-

ever, when it is realized that about 50 per cent of cancers occur in non-accessible sites (internal organs, etc.) and that the early recognition of small curable cancers in these sites is extremely difficult, the practical problem is obviously considerable. The sifting of a population of over 10 million persons in one state alone would require a medical and nursing force not available therein today; indeed, with a yield of only about one cancer per 1,000 "well persons" examined, the maintenance of interest and diagnostic acuity on the part of the corps of examining physicians would appear to be an aim insuperable.

The early diagnosis of accessible cancers (skin, breast, etc.) is more difficult than many persons appreciate. Even when surgically removed tissue is available, histological criteria are not always black or white. This point is well illustrated by Willis⁹ in the early chapters of his textbook on tumors.

Other observers⁷ have stressed the practical problems involved in any large-scale cancer detection center program, namely:

1. Long waiting periods before examination (up to nine months).
2. Extreme difficulty of maintaining competent professional staff.
3. Lack of uniformity or completeness of examination.
4. Tendency to syphon off all available funds for local cancer work, to the detriment of other parts of the cancer control program.
5. Perplexity of examiners and lay volunteer workers at the fact that no cancers may be found in the first several hundred persons examined.*
6. Absence of adequate follow-up to ascertain if those advised to secure treatment really did so.

Curphey⁸ has commented on the 5,279 female and 877 male persons examined by the five cancer detection centers in Philadelphia between 1944 and 1946. In this group 24 cancers were found, distributed as follows:

Females: Fourteen cancers of accessible sites (breast, cervix, skin); five cancers of inaccessible sites (fundus uteri, gallbladder and abdominal area).

Males: Five cancers of inaccessible sites (prostate, ileum and lung).

Curphey regarded only 14 of the 24 as salvageable, and concluded that: "Such a record is distinctly discouraging and establishes the fact that no matter how well organized and medically efficient the detection clinic be, there is little it can offer to the patient with inaccessible cancer at this time."

He calculated that the yield throughout the 240-odd detection centers in the United States is about one case per 100 patients with symptoms, and only one per 1,000 without symptoms. Further, the bulk of those detected were cancers of the skin, breast and cervix.

* Levin estimates that there are about 218 new cases of cancer per 100,000 population per annum in New York State. The annual incidence of four common types is approximately as follows: Breast 80, cervix 34, stomach 22, lung 16.

It has been stressed by Willis and others that about 15 per cent of cancers in males and 45 per cent of cancers in females involve accessible organs. In a paper presented before the annual meeting of the American Radium Society this year, the author reemphasized that *these tumors of accessible sites are the ones most often cured*. Ayre² has stated that: "In the female, if patients attending a physician for a routine cancer examination had no further examination than a simple cervical smear or scraping, a breast palpation and a rectal examination, more cancer would be detected per patient than with any other known system of cancer examination."

From the foregoing, it seems obvious that routine examination of apparently well persons yields too small a number of curable cancers to be a practical procedure at present. Examination of selected groups, such as adults over 55, might yield five cases per 1,000 (Levin⁶) but, if the inaccessible lesions were excluded, the yield would probably be closer to 2.5 per 1,000. Confining examinations to females would be a still more worthwhile procedure, from the statistical viewpoint.

It is believed that stimulating every physician to make his office a detection center for accessible tumors would be a most practical approach to the problem on a statewide basis at the present time.⁴ If every adult over 40 years of age were to have a simple physical examination (inspection and palpation) of five common accessible sites, annually, more cancer would be detected in a curable stage than by any other method at present available. These five sites are: Skin, lip and oral cavity, breast, cervix, rectum and rectosigmoid.

Such preliminary examinations need involve no laboratory work, x-rays, smears or other special tests. It is quite agreed that the results of properly performed cytologic studies of vaginal, bronchial, gastric and urinary secretions are sometimes a good clue to early cancer. However, such tests on a statewide basis are not yet technically feasible.

The "tumor clinic" is commonly spoken of as a place for the diagnosis and treatment of cancer. However, if most cancers are to be diagnosed early they must be sought when they are first detectable—in the practitioner's office. The practicing physician is the person whose interest we must hold in order to make significant advance. His is the best, most widespread and most economic "detection center."

MULTIPHASIC SURVEYS

It has been stated, with reason, that cancer is only one of the disabling entities of age, and that the periodic detection examination should include a check for hypertension, articular disease, pulmonary tuberculosis and diabetes, in addition to routine urinary and serologic tests. On a small scale, such procedures seem feasible. Statewide, it is not readily apparent how they could be achieved with maintenance of any degree of diagnostic quality or accuracy.

FREQUENCY OF RECHECK

If periodic detection examinations are in order, how often should they be repeated? Kirklin⁵ has shown that quarterly roentgenologic studies would be necessary to detect early gastric cancer. Sante⁸ has observed that chest surveys should probably be repeated quarterly to be of value as a representative picture. If repeated on a mass scale every three months they "would soon become one of the principal enterprises of the nation." For practical purposes, an annual recheck of accessible sites would appear to be the most feasible approach at the moment.

POSSIBLE ALTERNATIVE PROGRAMS

If cancer detection centers are not practical or worthwhile, what then should be done? Several years ago, Ackerman¹ suggested one alternative as follows: "Without disrobing the cancer detection clinics of the nobility of their aims, it may be justly considered whether the effort and expense cannot be put to better service in increasing and sponsoring the facilities for training of specialists (tumor pathologists, radiotherapists, and surgeons) on the skill of whom the therapeutic results will greatly depend." If the author might comment on this, he would stress the great need for additional numbers of tumor pathologists.

Therefore alternative number 1 for the American Cancer Society might be an intensive program to secure more qualified pathologists throughout the country. Number 2 would be to aid state medical associations to encourage their members to make *every physician's office a detection center*. Number 3 could be to support all bona fide voluntary health insurance plans to the end that every potential cancer patient is able to arrange for *his own medical and hospital care*, if and when needed.

The Cancer Society has taken the lead in public education on cancer, and has greatly aided research and professional education in cancer. Can it now direct the detection program along more evolutionary lines?

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Physiologic Basis of Nasal Operations

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SUMMARY

To be successful, intranasal operations must be so designed as to restore the normal physiologic function of the nose. It is impossible with impunity to operate upon the interior of the nose as though it were simply an air flue and on the sinuses as though they were boxes.

As the object of nasal operations is to restore, as far as possible, normal physiologic conditions within the nose, an understanding of the physiology of the nose is a prerequisite of such procedures. Unfortunately, some phases of nasal physiology remain unknown. However, if that which is known were applied, the results of nasal operations would be better.

Major functions of the nose include: (a) serving the sense of smell, (b) furnishing a passage for the air on its way to the lungs, (c) conditioning the air for reception in the lungs by warming, moistening and cleansing, (d) destroying bacteria and possible viruses, and (e) acting in a self-cleansing capacity. All of these functions must be borne in mind by the surgeon, so that, for example, when he must restore an air passage mechanically, it will be done in such a way as not to hamper self-cleansing or impair humidification.

EXTERNAL NOSE

Deviations of the external nasal pyramid may be such that they result in obstruction within the nose. When such obstruction is present, the cause can frequently be demonstrated with ease. The plastic procedure for the relief of the condition entails a bilateral osteotomy and replacement of the nasal pyramid in the midline. When this is done, often some adjustment in the septum must be made.

The bridge of the nose is subject to deformities in the form of humps, which are usually symptom-free, and saddle depressions, which may be productive of symptoms. Some rhinoplastic surgeons claim that breathing is often improved in cases of saddle depressions by the insertion of a graft along the bridge of the nose.

Operations to correct deformities of the lobule of the nose are largely for cosmetic purposes and need

not be discussed, except to state that every effort should be made to preserve the cartilages and other structures in a condition as nearly physiologic as possible.

Deformities of the nostrils and alae are more commonly of importance. Embarrassment of inspiration may result from anterior nares which are too small, too narrow or placed in an improper plane, as well as from alae which are too thin and soft so that they collapse easily. If the nostrils are too small, because of thickening of the alae or columella, this can be remedied by removal of portions of these structures. If the columella is to be thinned down, an incision can be made just within the vestibule on one side, parallel with the margin of the columella, and enough of the fibrous tissue within the columella removed to reduce its thickness considerably and thus increase the size of the anterior nares. Sometimes it is necessary to remove a portion of the medial crus of the alar cartilage. Alae which are too thick may be made thinner by making two incisions parallel with the lateral margin of the nostril, and removing the wedge of tissue between them.

When the tip of the nose is long and pendulous, the plane of the anterior nares may be such as to direct the jet of inspired air too high and too far anteriorly. Although this may not be of great importance, it may be corrected easily by a plastic procedure shortening the nose.

VESTIBULE

There is a valve-like action in the vestibule of the nose during inspiration which is thought by some to be the most important nasal function. The width of the vestibule, during quiet respiration, remains about the same on inspiration as on expiration; but, in forced inspiration, the upper portion of the vestibule (limen nasi) sinks in toward the septum in such a way as to cut down the flow of inspired air, thus increasing the negative pressure within the chest. During this action the upper lateral cartilage sinks in toward the septum at the same time that the upper margin of the alar cartilage, with which it is connected by an aponeurosis, tips medially and inferiorly.

The resistance produced by this valve action to inspired air Foman* believes is necessary for the normal growth and development of the face and chest. If a child is a habitual mouth breather, and lacks this resistance, the facial bones become deformed, the nose narrowed, the hard palate rises

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*Foman, S.: Personal communication.

high and the chest is apt to be malformed. Resistance to inspired air increases negative pressure in the tract behind the vestibule and increases the negative pressure within the thorax. Foman states that the negative pressure during inspiration aids in bringing the blood down from the vena cava into the right heart and also aids in the pulmonary circulation. This is conceivable, since the valves in the veins hold the column of blood against the expiratory positive pressure. Often, on inspection of the vestibule, the septum is found to be too wide between the two limina nasi, and, during forced inspiration, the lateral wall of the vestibule collapses against the septum, obstructing the inspiratory air flow and causing considerable inconvenience to the patient. In these circumstances, the septum in the vestibule must be reduced in thickness. There are often thickened bony and cartilaginous ridges in this portion of the septum; removal of these, together with thinning down of the septum, often promotes easier respiration, simply because the vestibules have been widened. However, it must be borne in mind that a certain amount of resistance is normal and the aim of the operation should not be to make the vestibule as wide as possible but to give sufficient space so that the resistance is not abnormally great.

SEPTUM

The ideal septum has usually been considered to be one which is straight, thin, and lying exactly in the midline. The ordinary submucous operation is designed to make such a septum. However, the normal septum is by no means always perfectly straight, nor is it uniformly thin. The quadrilateral cartilage is normally much thicker than the perpendicular palate of the ethmoid and there is often a more or less normal ridge on the lower portion of the septum, which follows the line of the vomer bone. The cartilaginous portion of the septum is frequently slightly deviated toward one side or the other. A septum should not be judged to be abnormal just because certain irregularities can be seen in it. Frequently, when a test is made, the air will be found to flow smoothly and freely and breathing will be perfectly normal and equal on both sides. If this is the case, operation is not indicated.

Presumably, the purpose of the septum is to keep the flow of air through the nose smooth, and, at the same time, by virtue of the swell bodies contained in it, to control the width of the air passages. Often, when a septum is deflected toward one side or the other, there is a compensatory enlargement of the middle turbinate on the side of the concavity. A submucous resection on such a septum could disturb a nose which is otherwise functioning well, creating an obstruction on the side of the enlarged turbinate by bringing the septum too close to the turbinate. Surgical correction is necessary for a badly warped or deflected septum which is producing obstruction on either side. The operation selected will depend upon the deformity. If the entire

quadrilateral cartilage is involved, it is desirable to do a more or less complete submucous resection of the cartilage and often of the vomer and the perpendicular plate of the ethmoid as well. If the deformity is confined entirely to the cartilage, it is not necessary to disturb the bony portions of the septum. Sometimes practically the entire cartilage, including the antero-inferior margin in the columella, must be removed. Such extensive removal is liable to result in saddle deformity of the bridge of the nose, or in retraction of the columella, or both. This is due to contracture of the sheet-like scars which form between the two flaps, rather than to loss of support of the bridge, as was taught in the past. Such contractures can be largely obviated by the insertion of cartilaginous grafts between the flaps. When the scar tissue then contracts, the force of the pull is exerted against the cartilaginous grafts and not against the bridge of the nose.

The tendency during the past 25 or 30 years has been to do a complete submucous resection for practically any type of septal deformity. Recently, in septal surgery, there has seemingly been a tendency toward a degree of conservatism which 30 years ago saw rhinological surgeons sawing off spurs and ridges which were obstructing the nasal passages, rather than doing complete submucous resections. This was good as far as it went and constituted an attempt to restore the normal air passage. However, it was often inadequate because the septum itself was usually warped and buckled. If the septal deflection is due to dislocation of the inferior margin of the cartilage, so that it overrides the bony ridge on either side, it can be restored to normal position by means of reduction of the deformity rather than a complete submucous resection. Such operations are correct in principle in that they restore the normal physiologic condition of the nose, but they must be adequately performed.

Sometimes the antero-inferior margin of the septum is deflected in such a way that it obstructs the vestibule on one side, making it necessary to remove the lower portion of the septal cartilage. Drooping of the tip of the nose may result on account of subsequent scar contraction unless a cartilaginous graft, or strut, is placed within the columella in such a way as to resist the scar contracture and prevent drooping of the tip.

TURBINATES

The turbinates are important physiologic structures, acting both as radiators of heat and as humidifiers. Removal or destruction of large portions of the turbinates results in a dry nose and a great deal of chronic difficulty. A generation ago there were much more extensive operations done upon turbinates than at present. Most rhinologists now seem to understand well that the physiologic function of the turbinates cannot be destroyed with impunity, and operations have become much more conservative.

It is possible for the turbinates to lie too close to the septum, interfering with the inspiratory air flow,

or too close to the lateral wall, hindering sinus drainage, under certain inflammatory conditions. Either of these abnormalities may be remedied by fracturing the turbinate in the required direction. This is a minor operation and does not disturb the physiology of the nose.

Partial resection of an extremely hypertrophic turbinate may be justified, but even this must be done with caution because sometimes a turbinate may be enlarged to compensate for a deflection in the septum. Often these turbinates contain an air cell, which is usually normal and should not be disturbed unless the turbinate is actually causing obstruction.

In dealing with the turbinates these two principles should be kept in mind: (1) the channels through which the incoming air flows are normally narrow and the surgeon must avoid making them too wide; (2) the air flow should be maintained in normal channels and should not be shunted into portions of the nose where the mucous membrane is unaccustomed to the force of the inspiratory air blast—for instance, in the meatuses.

The author did a series of experiments on rabbits and dogs quite a number of years ago which indicated that severe injury may be done to delicate mucous membranes if they are abnormally exposed to the drying action of inspired air. For example, in rabbits, by closing one nostril surgically, the character of the mucous membrane can be altered on both sides. On the open side, where double the normal volume of air passes, the mucous membrane tends to become squamous-like. On the closed side, certain other pronounced changes take place. It does not necessarily follow that the same thing would happen in man. In congenital atresia of the choanae, the nasal mucosa has been found to be nearly normal. On the other hand, most experienced rhinologists have seen the distressing drying and crusting which follow extensive removal of turbinates. It is prudent not to deflect air flow into the meatuses, against the ostia of the sinuses or into the sinuses themselves.

The turbinates should be preserved intact as far as possible. Sometimes they can be reduced in size by treatment with cautery. The hypertrophy of a turbinate which is enlarged for its full length can be reduced by passing a diathermy knife along the entire length of the turbinate, parallel with the inferior margin. It should be passed fully down to the bone in order that resulting scar tissue may extend from the surface to the bone, and, as it contracts, cause a corresponding reduction in the size of the hypertrophy.

SINUSES

The function of the sinuses is unknown and perhaps they have none. Proetz gives some evidence to support his view that they may be developmental accidents. Many functions have been assigned to the sinuses, but none has ever been proved, other than that each sinus is an efficient self-cleansing organ. The ciliary mechanism within it is rather elaborate

and cannot be disturbed a great deal without causing pathologic changes within the sinus. Whether they have a function or not, the sinuses do exist and must be reckoned with. They do become infected at times and surgical intervention may be necessary. Because the sinus mechanism can be so easily deranged, any operation attempted should be aimed at either one of two extremes: To restore the normal physiologic conditions or to remove the organ entirely, by amputation as it were. Middle-of-the-road measures may be worse than useless.

The old concept of sinus operations seemed to be based largely on gross anatomy and the physics of gravity. The rhinologist sought drainage and ventilation. By "drainage" he meant making large holes, preferably in dependent portions of the sinus; and by "ventilation" he meant exposure of the sinus to the atmosphere. However, sinuses do not drain normally by gravity nor are they normally exposed to the air. The normal air exchange through the ostium of the sinus is minute and the normal drainage passes through the ostium without reference to gravity. The ostium may be located in the highest portion of the sinus. Hence operations done in accord with the former concept often led to the formation of bands, folds and rings of scar tissue which interfered with drainage; sometimes such scars formed pockets which then became infected. Windows, which were made for drainage, often closed and effective drainage was made impossible. Meanwhile the patient suffered from continuous discharge, and the condition after operation was frequently worse than before.

EXPERIMENTAL WORK

The author did some experiments designed to demonstrate the results of surgical interference with the sinuses. In one series on the frontal sinuses of dogs, the mucous membrane at the ostium was partially removed, leaving a ring of denuded bone. This resulted almost invariably in complete closure of the ostium, thus cutting off the sinus from the nose and indicating that the surgical procedure of enlarging an ostium by curettage is wrong in principle. In other experiments, the removal of strips of mucous membrane from curved surfaces within the sinuses resulted in crescentic scars which interfered more or less seriously with drainage. Such scars might easily result from curetting of sinuses, without complete removal of the mucous membrane, and they could interfere with drainage even though they did not close the sinus or even narrow it appreciably. If these scars merely lay transversely across the line of ciliary streaming, they might interfere with drainage and cause accumulation of secretion.

Another series of experiments, designed to study the causes of closure of surgical windows, was done on the septum between the two frontal sinuses in dogs. It was found that the window would often close if its margins were left remaining as a ring of denuded bone. However, if the operation was done in such a way that the mucous membrane was

conserved on both sides and brought together across the denuded margin of bone, then the window would remain patent, with a minimal amount of contracture. Continuing the same line of thought, other experiments were done in which a ring of mucous membrane was removed from the complete circumference of the interior of the frontal sinuses of dogs. The bone was not injured in any way. Such denuded bands resulted in the building up of stenotic scars, which, in some instances, became so extreme as to form a complete wall dividing the sinuses into two portions. It has been taught that the closure of a surgical channel from the nose into the frontal sinus is due to collapse of soft parts and that if there were rigid bone on all sides of the channel, it would not close because it could not collapse. In the light of these experiments, this teaching would seem to be in error because closure can occur no matter how rigid the walls may be.

Further experiments were made on the maxillary sinus of the rabbit. In this animal the sinus lies conveniently close to the nasal wall for its full length, and it is possible to make a window between the nose and the sinus at various positions with reference to the ostium. A window can be made far from the ostium, or very close to it, or it can be made to include the ostium. The bone is extremely thin in this wall and it is easy to make the window stay open. It was found that windows made far from the ostium did not greatly disturb the normal physiology of the sinus and the sinus remained clean. However, the closer to the ostium that the window was made, the greater the disturbance which resulted. When the ostium itself was enlarged, the sinuses invariably filled with secretion which became infected. If the window were made midway between what might be called the fundus of the sinus and the ostium, an interesting phenomenon resulted. That portion of the sinus lying distal to the window would become filled with secretion and might become infected, whereas the rest of it, which had the ostium available for drainage, remained clean. The drainage mechanism of the sinus is deranged not only by an obstructing or stenotic scar, but, in some cases, merely by interrupting the continuity of ciliary flow. In such instances it was noted that the mucus which drained from the distal portion of the sinus was carried to the window margin by ciliary action and there it stopped, even though the distance across the margin of the window to normally active ciliary drainage in the nasal space was only a millimeter.

Another group of experiments was done on the dog to study the result of complete removal of the mucous membrane from the sinus with the exception of that lining the ostium. Many of these sinuses became almost completely obliterated and filled with scar tissue. Some became partially restored by mucous membrane growing in from the ostium. In these, the drainage seemed good and the sinuses remained clean. Invariably there were cysts in the scar tissue which formed and it was thought that the mucous membrane had not been cleanly re-

moved from the bone. Undoubtedly, this was the cause in some instances, but in others the cysts were found at some distance from the bone, deeply buried within the scar tissue, leading one to speculate whether perhaps these were transplants of mucous membrane accidentally lost during the manipulation.

A few rabbits were operated upon to test the possibility of transplanting sinus mucosa. Some epithelium (mucoperiosteum) removed from the maxillary sinus was placed into drill holes in the skull in the region of the occiput. Cysts resulted from these transplants which looked very much like those found in the scar tissue in the frontal sinus in the dogs. The cysts were filled with mucus and lined by ciliated epithelium. The ciliary streaming in some of the cysts found in dogs was very active.

It can be seen from these experiments that the sinuses cannot, with impunity, be treated surgically without reference to their physiology. It is not to be expected that large holes made in sinus walls, without regard for the specific mechanism involved, will remain open and drain the sinus freely ever after. Denuded areas of bone will become covered with scar tissue, which may interfere a great deal with nasal drainage and physiology. The scars will take form depending upon the size and shape of the surface on which they develop.

PRINCIPLES OF SINUS OPERATIONS

The four principles in sinus operations, as laid down by Proetz,* have as their objective: (1) the preservation of the sinus as a functioning organ, (2) the preservation of the ostium, (3) the protection of the ostium from direct blasts of air and (4) the protection of the cavity itself from air flow. To these might be added the two principles of (a) making drainage windows as far from the ostium as possible and (b) leaving no wide ring-like areas of denuded bone around the drainage channels.

The antrum window, as usually made in inferior meatuses, follows these principles rather well. The sinus remains as a functioning organ. The ostium is untouched and both the ostium and the interior of the cavity remain protected from air blasts. The window is far enough from the ostium so that it does not interrupt ciliary streaming materially. When the window is made, it will stay open if the opening in the bone is cut a little larger than that in the mucous membrane, on both the nasal and sinal sides, thus allowing the mucous membranes on the two sides to meet over the bone.

Proetz has designed a window into the sphenoid sinus which follows these principles. The mucous membrane over the rostrum is incised close to the septum, then a vertical window is made through the bone into the sinus, extending from the thick bone above to the thick bone below, at the floor, and as close to the septum as possible. Such a window will remain open if the mucous membrane covers the denuded bony margin fairly well. It is some distance from the ostium, it does not interfere with the

* Proetz, A. W.: Personal communication.

normal drainage, and the sinus can be readily irrigated.

The most difficult problem is encountered in making a drainage opening into a closed frontal sinus. Sometimes this may not be possible. The author has treated two patients for a mucocoele of the frontal sinus which eroded through the floor into the orbit, causing a marked proptosis and downward displacement of the eyeball. In both of these cases, the cysts were some little distance away from the closest intranasal point. Both patients were successfully operated upon by carefully preserving the mucous membrane from the frontal sinus and from the ethmoids which were encountered, as well as from the nose. The bony trabeculae were removed and a bony channel formed, which was then lined by shaping into it the bits of mucous membrane which had been saved. In one instance the bits of mucous membrane

were simply packed into position, and in the other they were sutured together as in a rhinodacryocystostomy. The result was excellent in both. The problem is much more difficult, of course, if suppuration is present. It may then be necessary to amputate the sinus, as it were, by removing the entire lining. If this is undertaken, then all mucous membrane must be completely removed in order that no infected pockets or cysts may remain. However, the ostium should be preserved to drain any portion of the sinus which might reform.

There has been some advocacy for the use of skin grafts to line the surgical channel between the nose and the frontal sinus, but this would seem to be entirely unphysiologic because the skin and respiratory mucosa are different tissues and one would not expect that they could be used interchangeably.

Medical Arts Building.

CAUTION

The "Huggins" or "H.M.J." Test for Cancer

Numerous articles have appeared in the public press, magazines, and advertisements from commercial firms under the title "Simple Blood Test for Early Cancer Diagnosis."

These articles are premature. The test referred to is still in the laboratory phase and is not intended for routine use, or as an office procedure. Physicians are warned against accepting reports on this "simple test" as evidence of presence or absence of cancer.

The test is based upon thermal coagulation of serum proteins and is variously referred to as either the "Huggins" or "H.M.J." test.

DAVID A. WOOD, M.D., *Secretary*
California Medical Association Cancer Commission

Dihydrogenated Alkaloids of Ergot in Treatment of Peripheral Vascular Diseases

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SUMMARY

The dihydrogenated alkaloids of ergot, dihydroergocornine (DHO 180) and an equal mixture of dihydroergocornine, dihydroergocristine and dihydroergokryptine known as CCK 179 have been found to be therapeutic adjuncts in the medical treatment of peripheral vascular diseases. Their action is primarily that of adrenergic blockage, although depression of the brain stem is to be considered.

The mixture of alkaloids (CCK 179) was found to be more effective than a single alkaloid, dihydroergocornine (DHO 180). A greater number of patients were benefited, relief of symptoms was greater and the dosage easier to establish. A favorable therapeutic response of clinical significance with the mixture was obtained in approximately 60 per cent of all cases investigated. It was of greater benefit in the organic occlusive diseases, where a larger percentage of favorable responses was obtained than in the purely vasospastic disorders.

Orally and subcutaneously, CCK 179 exhibited vasodilating properties which compared favorably with paravertebral and peripheral nerve block, reflex heat, alcohol and sympathectomy. Surface temperatures were elevated, oscillometric readings increased and

tolerance to cold increased in a statistically significant number of cases. Effects of sympathectomies were frequently enhanced. Following subcutaneous administration, increased surface temperatures of the extremities of one to two hours' duration were obtained in 90 per cent of all cases.

Paresthesias, nocturnal cramps and intermittent claudication were improved. A sense of well-being was occasionally exhibited.

Blood pressure and pulse rates were rarely affected. Blood pressure was lowered in normotensive patients, but was rarely changed in hypertensive patients.

Symptoms of overdosage appeared after two to three months of continuous therapy. These were manifested by lowered surface temperatures, decreased tolerance to cold, return of intermittent claudication and occasionally by vague general discomfort. These symptoms disappeared on cessation of therapy. Improvement frequently followed. In only one case was there an immediate reaction. Following subcutaneous administration of CCK, blood pressure and pulse rate increased and oscillometric readings and surface temperatures decreased.

Frequent courses of therapy with interruptions were necessary for maintenance of improvement.

THE development of a therapeutically effective chemical vasodilator in chronic peripheral vascular diseases has been one of the goals of workers in the field. Several new vasodilating compounds, adrenolytic, sympatholytic and ganglionic blocking have been reported recently.⁹ Nickerson¹⁵ in a classical paper discussed the pharmacological activity of many of these compounds. He referred to their activity as adrenergic blockade.

The primary requirement of an acceptable agent is the inhibition of normal and pathological vasoconstriction in an affected extremity with the establishment of an enlarged arterial and capillary bed. Generalized vasodilatation of the entire vascular bed is to be specifically avoided. Ease of administration,

sustained action, lack of toxic or unpleasant side-effects and a high degree of therapeutic effectiveness are additional necessary requirements.

It is the purpose of this presentation to report on the therapeutic value of certain dihydrogenated alkaloids of ergot*¹⁶ which appear to have a beneficial clinical action in peripheral vascular diseases. The exact action of these drugs is in doubt. Some investigators^{3, 4, 8, 16} state that these dihydrogenated alkaloids (DH compounds) of ergot have, in man, two important synergistic actions, namely, (1) a manifest central nervous system effect of inhibition of sympathetic activity and therefore the reduction of vessel tone, and (2) a latent peripheral sympatholytic effect. Nickerson¹⁵ questions the interpreta-

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* Supplied through the courtesy of Sandoz Chemical Works, Inc., New York City, New York.

tion offered by these investigators of their observed results. He states that there is absence of evidence of significant adrenergic blockade and that the mechanism involved is depression of the brain stem rather than inhibition of responses to sympathetic nerve activity.

HISTORICAL BACKGROUND

The use of ergot in medicine dates back for centuries. It was known early to midwives for its oxytocic properties. Dale⁶ in 1906 was the first to recognize two active principles in ergot: (1) A direct stimulating action on smooth muscles, and (2) the inhibition of sympathetic activity. Rothlin¹⁶ showed that hydrogenation of various ergot alkaloids reduced their toxicity considerably. He found that, following hydrogenation, the ergotamine and ergotoxin groups showed a great increase in sympatholytic activity with little or no vasoconstrictive tendency. The clinical application of these alkaloids in the treatment of peripheral vascular diseases has been recent. Clinical improvement of patients has been observed by some investigators.^{7, 12, 13} Laboratory studies using the plethysmograph and surface temperature determinations have shown peripheral vasodilating activity.^{4, 5, 11, 17} Hafkenschiel and co-workers¹⁰ found that the abnormal resistance to blood flow in the hypertensive brain was reduced by dihydroergocornine. These studies have all been made with single dihydrogenated ergot alkaloids, chiefly dihydroergocornine.

METHOD AND MATERIALS

The following hydrogenated alkaloids were investigated: Dihydroergocornine (DHO 180), dihydroergocristine (DCS 90) and dihydroergokryptidine (DKH 135). Dihydroergocornine alone was studied initially. It was administered orally over a period of three to nine months to 45 patients. Later a combination of the three alkaloids was used. This combination was known as CCK 179. It was administered orally, subcutaneously and intra-arterially. The DHO 180 contained 1 mg. of active substance per cc.; the CCK 179 for oral administration contained 1 mg. of mixture of the three alkaloids in equal amounts (0.33 mg. per cc. of each), and the parenteral solution contained 0.3 mg. of mixture (0.1 mg. of each alkaloid) per cc. The oral solutions were tasteless and colorless. A transient burning sensation was present on subcutaneous injection.

Sixty patients were treated for from two to nine months with CCK 179. All types of peripheral vascular disorders were included in both studies. Most of the patients were started on 4 minims four times a day, and the dose was increased by 1 to 4 minims daily depending on the surface temperature rise. The majority required 4 to 6 minims per dose for maximal cutaneous dilatation. All subjects were tested under practically similar conditions. Subjects were rested in the recumbent position for 45 minutes to one hour with the extremities bare. The majority of patients were ambulatory; a few were

hospitalized. All other medication and therapeutic procedures were discontinued several weeks before starting this investigation except where specifically noted. A few patients continued to smoke. Those that discontinued smoking stopped a minimum of three months prior to the beginning of this study.

Surface temperatures, oscillometric readings, blood pressure, pulse rate, skin color, perspiration and respiration were recorded. Subjective symptoms were elicited. Electrocardiograms and eyeground studies were made on a few of the patients before and during therapy. Recordings under basal conditions were made in all cases. At least three weeks of observation was carried out before therapy was instituted. The great majority of the patients had been observed for many months and years. Frequent examinations were made before and during the investigation; patients were checked a minimum of eight times during a period of three months. Subcutaneous administration of CCK was frequently combined with oral administration.

All cases were chronic. None of the patients were improving prior to therapy. Many were regressing. Placebos were frequently used. Comparisons were made with results obtained with other vasodilating procedures such as posterior tibial and paravertebral sympathetic nerve blocks, tetraethylammonium chloride, reflex heat, alcohol and sedation.

The results of the investigation of dihydroergocornine (DHO 180) are listed in Table 1. The results of the investigation of the CCK mixture of alkaloids are listed in Table 2. Many of the patients were included in both studies.

TABLE 1.—*Patients Given Dihydroergocornine (DHO 180) Orally*

ARTERIOSCLEROSIS OBLITERANS: 25 patients, 15 males, 10 females, ages 55 to 76. Diabetes mellitus was associated in 9, hypertension in 4. Favorable results were obtained in 12.

VASOSPASTIC DISORDERS (Raynaud's disease and Raynaud's phenomenon associated with scleroderma, menopausal syndrome and hereditary cold fingers): 14 patients, 11 females and 3 males, ages 19 to 71. Improvement in 2.

THROMBOANGITIS OBLITERANS: 5 patients, all males, ages 44 to 55. Improvement in 4.

EMBOLIC OCCLUSION: Arterial, popliteal, chronic, 1 patient, female, age 44. No improvement.

TOTAL: 45 patients. Favorable response in 18 (40 per cent).

TABLE 2.—*Patients Given CCK 179 Mixture, Orally and Parenterally*

ARTERIOSCLEROSIS OBLITERANS: 36 patients, 27 males, 9 females, ages 55 to 76. Diabetes associated in 10, hypertension in 4. Improvement in 26.

THROMBOANGITIS OBLITERANS: 8 patients, all males, ages 40 to 55. Improvement in 7.

VASOSPASTIC DISORDERS (Raynaud's disease, Raynaud's syndrome associated with scleroderma, menopausal syndrome, trauma, scalenus anticus, cervical peri-arthritis and livedo reticularis): 16 patients, 15 females, 1 male, ages 19 to 53. Improvement in 4 cases.

TOTAL: 60 patients. Favorable response in 37 (60 per cent).

OBSERVATIONS AND RESULTS

The DH alkaloids were well tolerated. The CCK mixture was not only effective in a greater number of cases than dihydroergocornine (DHO 180), but the favorable clinical response in each case was more pronounced. The optimum dose of DHO 180 was difficult to establish and maintain. Individual variations were frequent. Although CCK dosage was fairly fixed—four to eight minimis (0.25 mg. to 0.50 mg. of active substance) four times daily—the duration of therapy was likewise subject to considerable individual variation. With oral medication, approximately one to three weeks of administration was necessary for favorable clinical improvement to appear. The majority required about ten weeks of therapy. Beyond this, favorable effects appeared to diminish. This observation has been confirmed by others.¹⁴ During the course of treatment, improvement was maintained and continued for two to four weeks following complete cessation of treatment. Patients felt better if the dosage was gradually reduced over a period of days rather than suddenly stopped. Frequent courses of approximately ten weeks' duration with intervening rest periods of two to four weeks gave the best results.

Effect on Surface Temperatures and Cold Protection. With dihydroergocornine, surface temperature rises with increased cold protection were obtained in 18 out of 45 cases. With CCK orally, a favorable response was obtained in 30 of 60 patients. The surface temperatures of the extremities were increased up to the 90 to 95° F. range with fair to good cold protection provided in the patients responding. Patients stated their extremities not only warmed up more quickly but remained warmer especially at night. The temperature rise was confined primarily to the extremities. With the temperature rise, the skin color became pink. No temperature rises were obtained in smokers. Temperature rises were not maintained consistently. There were occasional periods of fluctuation. These were of short duration and the reduction in temperature was never great.

Intermittent Claudication. Dihydroergocornine was ineffective. CCK orally resulted in a favorable response in 12 of 27 patients with arteriosclerosis obliterans and six of eight patients with thromboangiitis obliterans. The majority of these patients responding stated that although in walking they were forced to halt approximately the same number of times as prior to medication for the first block or two, after the third or fourth block they could go up to a mile with no discomfort during or after the walk. The pace was increased for these patients.

Healing of Ulcerations. CCK was of benefit in the healing of ischemic ulcers in five cases. These ulcerations were of long standing with absolutely no signs of improvement. Within ten days of CCK administration, evidences of healing were apparent. Progress was rapid thereafter. No new therapy was introduced other than the CCK. There was no bene-

fit in seven cases. Dihydroergocornine was found to be of no value in this respect.

Blood Pressure. Normotensive patients frequently showed a slight but sustained drop of 5 to 10 mm. of mercury in both systolic and diastolic blood pressure on oral medication of CCK. Hypertensive patients did not respond. Dihydroergocornine did not alter pressures significantly.

Oscillometer Determinations. The amplitude of pulsations was increased with CCK in a few cases in which cutaneous dilatation occurred. In some cases, in spite of considerable surface temperature rise, oscillometer readings remained unchanged. The maximum response was obtained in one patient with thromboangiitis obliterans in whom the increase of amplitude was over 200 per cent in all extremities.

Pulse Rate and Respiration were usually unaffected. Occasionally the pulse rate was slowed five to ten beats.

Electrocardiograms. Only a few observations were made. No significant changes were apparent.

Eyeground Studies. Pronounced dilatation of the retinal vessels appeared in a small number of cases following subcutaneous injection of CCK. However, this was not a consistent finding.

Pain. Ischemic neuritis and rest pains were rarely modified in any way.

Miscellaneous. Paresthesias and nocturnal cramps were relieved in a few patients. A pronounced sense of well-being was noted by four patients on CCK. Persistent edema of the hands was relieved in two patients on CCK. Perspiration was rarely modified.

Comparisons with Other Vasodilating Procedures. Six patients received, in addition, tetraethylammonium chloride (Etamon[®]) intravenously and intramuscularly during a period of hospitalization. Two patients, females, ages 22 and 24, suffering from Raynaud's disease with severe vasospastic symptoms in whom cervical sympathectomies had been done a few years previously, were unchanged regardless of therapy. One patient, a nurse aged 22, who had a scalenus anticus syndrome with vasospastic symptoms in the affected extremity, also had no response to any preparation. One patient, female, aged 60, with marked peripheral autonomic instability and severe pain and edema in the hand following a fracture of the humerus six months previously, was completely relieved with CCK orally but unaffected with Etamon. Two patients, females, ages 22 and 53, with generalized scleroderma and Raynaud's syndrome for which cervical sympathectomies had been performed a few years previously, were unaffected with Etamon and dihydroergocornine. Pronounced warming of the extremities occurred on CCK orally.

Two patients in whom paravertebral block did not elicit temperature rises responded to CCK orally. One of these two patients, a male, age 53, seven months previously had had deep laceration of the volar aspect of the left wrist which severed the ten-

dons, nerves and arteries to the hand except for a small branch of the radial artery. The hand was shiny, cyanotic, icy cold and edematous. Function was limited. Following a cervical block, Horner's syndrome developed, the extremity became hot and dry to the wrist, but the hand and fingers were unchanged. CCK subcutaneously on two occasions was followed by an increase in temperature of the fingers and the development of a normal pink color. The temperature of the thumb rose to the 90-95° F. range but that in the other fingers rose only to the high 80's from a previous 70 to 75° F. range. On oral CCK only slight temperature rises were apparent, but the edema of the hand subsided completely. The other patient was a male, aged 68, who had severe arteriosclerosis obliterans with occlusion of the lower abdominal aorta. Paravertebral block revealed no temperature rise. On oral CCK, there was a temperature rise of 5 to 8° F. to the high 80's, which compared favorably with the highest temperatures obtained by alcohol and reflex heat. In no case did CCK subcutaneously or orally prove as effective as a posterior tibial block in obtaining the maximum temperature rise. In the majority of cases, the rise with CCK subcutaneously was good. It was usually 2 to 3 degrees below the maximum obtained by nerve block. In only a few cases of organic occlusion was the block successful and the CCK without effect. CCK orally was found to be as effective as alcohol and reflex heat in the majority of cases studied.

Results in Sympathectomized Patients. Six patients who had had sympathectomies were given dihydroergocornine orally and CCK orally and subcutaneously. Two of the patients had Raynaud's disease and the sympathectomies had been ineffective. DH therapy was likewise ineffective. Two patients with scleroderma responded to CCK with temperature rises to 90-93° F. from previous lows of 70-80° F. Edema of the hands and fingers in one case was relieved. In one patient, a male, aged 50, with thromboangiitis obliterans, upon whom bilateral lumbar sympathectomy had been performed many years previously, no significant differences were noted with CCK. One patient, a male aged 50, with thromboangiitis obliterans had had unilateral lumbar sympathectomy two years previously. Both DH compounds were effective in raising the surface temperatures of extremities on either side. The intermittent claudication disappeared only with CCK. The surface temperatures in the lower limbs became about equal, and in the 90's, while the patient was under therapy.

CCK Mixture Subcutaneously. CCK was given by subcutaneous injection to 45 patients. In 40 patients, the temperatures of the fingers and toes rose to the 90° F. and 95° F. range, whereas previously they had been below 90° F. The increase occurred at about 45 minutes after the injection, reached a peak in 60 to 75 minutes and decreased to previous norms in 90 to 120 minutes. Color was improved. Blood pressure, pulse rate and oscillometric readings were

rarely affected. All types of cases were included in this series.

Intra-arterial Therapy. CCK was administered intra-arterially on three occasions to two patients. These patients had shown no response to posterior tibial block and showed no response to the intra-arterial injection.

Reactions. A reduction in surface temperature was noted in many patients during the course of therapy. Whether this was due to too large a dosage, prolonged administration of small dosage with possible accumulation, or to a counter-regulatory mechanism could not be determined. Reducing the dosage or cessation for several days to two weeks brought on a return of the increased surface temperatures. One patient, a female, aged 55, who had coronary artery disease with old infarction and mild decompensation, hospitalized at the time of this study for severe arteriosclerosis obliterans and ulceration of a toe, was given 1 cc. of CCK subcutaneously. Within an hour, the temperatures of the toes and calves decreased 4 to 6° F., the blood pressure increased from 130 mm. of mercury systolic and 90 diastolic to 150 mm. systolic and 100 diastolic. The pulse rate increased from 88 to 96 and the oscillometric recordings at the wrists and ankles decreased. The hands, fingers and face became covered with perspiration. These symptoms disappeared within two hours of reaching their maximum. The patient was later treated with CCK orally and responded favorably.

DISCUSSION

The evaluation of any new therapeutic agent for chronic illness is difficult. The value of vasodilator drug therapy in the chronic peripheral vascular diseases has always been a subject of dispute. The Mayo Clinic Group,¹ in listing the pharmacologic agents recommended for peripheral vascular diseases, noted the plethora of agents and the lack of therapeutic effectiveness of the majority of them. Many drugs were found to have limited or even no value in the hands of others than the original investigator. The contributing factors modifying the course of chronic disease processes are many. In this presentation, the factors of spontaneous improvement, regression and associated therapy were considered in evaluating the results obtained. The majority of patients in this series had been under observation for periods up to ten years and the effect upon them of other therapeutic agents and procedures had been thoroughly investigated. They were all in a stationary period or getting worse; none were improving. It is felt, therefore, that in these circumstances fairly sound conclusions are permissible.

The dihydrogenated ergot alkaloids appear to act by adrenergic blockade resulting in a reduction of sympathetic tone with relaxation of the vessel wall. Nickerson's¹⁵ explanation of depression of the brain stem must also be considered. Regardless of the mode of action, an enlarged peripheral arterial and capillary bed was demonstrated in many of the pa-

tients showing favorable clinical response. The peripheral vessels in a normal individual are in a constant state of vasoconstriction necessary for the maintenance of body temperature. This is controlled through the vasomotor centers in the medulla.² In a patient who has peripheral vascular disease, this function is maintained. The normal vasoconstriction superimposed upon an organic arterial occlusion aggravates the ischemic process. Reduction of this tone, therefore, will aid in increasing the capacity of the arterial bed. As vasoconstriction is normally more pronounced in the lower extremities due to the factor of posture, and as the peripheral arterial occlusive diseases are more common in the lower extremities, reduction in tone in this area should result in a favorable clinical response. Clinical observations support this. Increased tone or spasm due to organic irritation from atherosomatous plaques or thrombi is an additional factor. This likewise was favorably influenced in many of the patients in the present series. It could not be determined whether this was due to a peripheral sympatholytic action or to an inhibition of the spinal sympathetic centers.

The reduction of hypertension reported by other investigators^{7, 8, 11} was not found. Wide differences in the method of administration and dosage are probably the chief factors. Most of the investigators have reported on the intravenous administration of the DH alkaloids and on the large doses necessary for oral administration.

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Endometriosis

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SUMMARY

The cause of endometriosis is not known. The incidence of the disease is greater than was previously suspected and it probably is increasing. Nulliparous women are more likely to have endometriosis than are women who have had children.

The commonest symptoms are lower abdominal pain, disturbance of menstruation, and dysmenorrhea, most often of the increasing or acquired type. Relative and absolute sterility are common partners of endometriosis.

A better percentage of correct preoperative diagnoses should be obtained in view of present knowledge.

Radical operation on women in the premenopausal age groups with endometriosis is resorted to in far too high a percentage of cases. The good results which can be attained with conservative therapy, including surgical and hormone therapy, should be stressed.

There is some evidence that endocrine therapy may control endometriosis. The dangers attending these methods have not as yet been determined.

THE purpose of this presentation is threefold: First, to emphasize the need of a continually thoughtful mind in diagnosing endometriosis. Second, to emphasize the importance of conservation of ovarian tissue in the premenopausal woman. Third, to review the problem as presented by a study of 153 patients operated upon in a small general hospital with a staff composed of specialists in obstetrics and gynecology, general surgeons and general practitioners.

There were 153 cases of proved endometriosis in this series taken from 2,660 cases of gynecological operations performed from January 1945 through January 1948. Thus the incidence was 5.7 per cent. This varies from some reports such as that of Meigs¹³ which was based upon private practice, but agrees essentially with the percentage he reported with regard to clinic patients and also with many other reports of similar studies. In the present study many cases had to be discarded because of lack of pathological confirmation, although the clinical description was classic. This point is important. Many times implants are not removed. It is the author's opinion, and one shared by many observers, that in the class of patients studied here the reported incidence in this series is far below the actual incidence.

Presented before the Section on Obstetrics and Gynecology at the 78th Annual Session of the California Medical Association, Los Angeles, May 8-11, 1949.

Endometriosis is definitely or seemingly increasing. Interest and knowledge are leading to more accurate diagnosis. Meigs¹³ reported with regard to patients treated by him in private practice that 35 per cent of those upon whom operation was done had endometriosis. As this percentage applies only to patients operated upon, many minor cases of this disease thus are not included. Fallon,⁴ reporting on observations of patients in a clinic, said that endometriosis was more common than acute appendicitis.

The incidence in the population at large is unknown, and because of pronounced variations between reports in the present literature, it is impossible to obtain a close estimate. In a recent article Beecham¹ reported the incidence of endometriosis in 1,000 consecutive gynecological office cases as 5.8 per cent.

The early symptoms of endometriosis are vague and in many cases a biopsy to make a positive diagnosis does not seem warranted. Thus the true incidence is unknown. Suffice it to say that the disease is more prevalent than was previously suspected.

In the present study the 153 cases were divided into the common classifications (as shown in Table 1):

1. Internal, or confined to the uterus — the so-called adenomyoma.
2. External, or found in the pelvis not involving the uterus.
3. Combined, involving both uterus and pelvic or other structures.

TABLE 1.—Incidence of Types of Endometriosis

Type	Number	Per Cent
Internal	60	39.2
External	83	54.3
Combined	10	6.5
Total	153	100.0

The incidence of the various classifications in various age brackets is shown in Table 2. The predominance of all cases lies in the age group from 30 to 55. In analyzing this table it is observed that adenomyosis occurs in a slightly older group of individuals than does external endometriosis. The incidence as reported here shows that the predominance of cases of internal endometriosis occurs in the age group from 35 to 55, while that of external endometriosis occurs in the group from 25 to 45. This confirms data noted by other observers.

In discussing statistics gathered in study of the 153 cases in the present report, an attempt will be made to elucidate the present-day opinions and views of writers relative to symptoms, signs, diagnoses, and treatment.

As revealed in the statistics of Table 3, there were

no specific symptoms of endometriosis. Ordinarily there was pain in the area involved, but even this was not constant. Dysmenorrhea was noted in 28.8 per cent of the patients in this series, as shown in Table 4. This was ordinarily of the increasing type. This figure corresponds well with that reported by Meigs¹³—26.4 per cent. Fallas and Rosenblum³ in a study of a similar nature reported an incidence of 43.4 per cent. The reported incidence of dysmenorrhea varies, depending upon the accuracy with which records are kept, but all observers record it as high. In the present series it will be noted that dysmenorrhea was more often associated with external than with internal endometriosis. This agrees with data reported by Fallas and Rosenblum and other observers.

Although dyspareunia is a symptom often associated with endometriosis, this is not revealed by the average record. It has been noted by the author

and reported by others that close questioning of patients elicits information showing that the incidence is much higher than would be indicated in the perusal of hospital records. Endometrial nodules in the posterior cul-de-sac are most often painful to pressure.

Symptoms of bladder involvement are usually, as reported by Henriksen⁶ and McDougal and Deur,¹¹ frequency and dysuria occurring prior to the menses and continuing through it.

The other symptoms noted may be explained by associated pathological conditions in the particular organ involved, as shown in Table 5. Here it is noted that fibroids of the uterus occurred in 29.4 per cent of cases. Other observers have noted a somewhat higher incidence of this associated condition: Fallas and Rosenblum,³ 41.5 per cent; Novak¹⁴ 33.7 per cent. The most common associated pathological conditions were found in the ovary; the highest in incidence were simple follicular cysts—30.7 per cent. Thus, rather high incidence of endometrial hyperplasia might have been expected. The high incidence of associated pathologic change in the ovary undoubtedly partially explains the high percentage of irregular and profuse bleeding previously noted under symptomatology. Unfortunately, there was no specific report on the endometrium in most of these records. Novak and Alves de Lima¹⁴ recently reported a study relative to the incidence of changes in the ectopic endometrium as compared to the uterine endometrium. They reported endometrial hyperplasia in 23.4 per cent of the cases studied.

The high incidence of hyperplasia and perhaps anovulatory cycles may be a partial explanation of the relative sterility noted in patients with endometriosis.

In Table 6 the incidence of involvement of organs is shown, and the data agree in general with the findings in studies by others with regard to the average anatomical locations of endometriosis.

TABLE 2.—Age of Incidence by Type of Endometriosis

Age	INTERNAL		EXTERNAL		COMBINED	
	No.	Cases	No.	Cases	No.	Cases
	Per Cent		Per Cent		Per Cent	
15-19..	0	0	0	0	0	0
20-24..	0	0	8	9.6	0	0
25-29..	1	1.7	11	13.3	0	0
30-34..	2	3.3	22	26.5	80.8%	0
35-39..	13	21.7	16	19.3	3	30
40-44..	11	18.3	18	21.7	3	30
45-49..	15	25.0	7	8.4	1	10
50-54..	12	20.0	1	1.2	2	20
55-59..	4	6.7	0	0	1	10
60-64..	2	3.3	0	0	0	0
65-69..	0	0	0	0	0	0

TABLE 3.—Symptoms of Endometriosis

Complaint	Type of Disease			
	Internal	External	Com-	Total
		binated	Per Cent	
Menorrhagia	23	16	4	43
Metrorhagia	12	10	1	23
Polymenorrhagia	0	1	0	1
Uterine hemorrhage	2	0	2	4
Dysmenorrhea	13	31	0	44
Lower abdominal pain	13	47	6	66
Backache	15	10	2	27
Abdominal tumor (noted by patient)	2	7	1	10
Vaginal discharge	6	7	1	14
Bladder symptoms	10	2	0	12
Rectal pain	0	2	0	2
Menopausal bleeding	5	0	0	5
Gastrointestinal upsets ..	0	1	1	2
Dyspareunia	0	6	1	7
Sterility	3	10	0	13
General menopausal symptoms	6	3	1	10
Chronic abortion	0	1	0	1
Pain in legs.....	3	1	0	4

TABLE 4.—Incidence of Dysmenorrhea in Endometriosis

Type	No. of Patients	No. with Dysmenorrhea	Per Cent
Internal	60	13	21.7
External	83	31	37.4
Combined	10	0	0
Total	153	44	28.8

TABLE 5.—Associated Pathologic Conditions

	Type of Disease				Per Cent
	Internal	Exter- nal	Com- bin- ed	Total	
	Number of Cases				
Fibroid uterus	23	21	1	45	29.4
Ovarian disease:					
Simple follicular cysts.....	17	27	3	47	30.7
Lutein cysts	4	4	1	9	5.9
Multilocular cystadenoma	0	2	0	2	1.3
Hemorrhagic cysts (not chocolate)	6	10	1	17	11.1
Carcinoma, ovary	0	0	1	1	.65
Dermoid cysts	1	0	0	1	.65
Fibromas, ovary	0	1	0	1	.65
Chronic pelvic inflammatory disease	5	18	1	24	15.7
Endometrial hyperplasia	8	5	2	15	9.8
Chronic appendicitis	3	8	1	12	7.8
Acute appendicitis	1	0	1	2	1.3
Endometrial polyp	1	6	1	8	5.2
Cervical polyp	0	1	0	1	.65
Pregnancy, intra-uterine	1	0	0	1	.65
Carcinoma, body uterus	2	0	0	2	1.3
Uterus bicornis unicollis	0	2?	0	2	1.3
Chronic cervicitis	19	10	3	32	20.9
Endometritis	0	0	1	1	.65

There were no cases of the rare locations (such as arm, leg, or pleura) noted in the records of the 153 cases here reported upon.

DIAGNOSIS

The early diagnosis of endometriosis within the pelvis or abdominal cavity presents one of the most difficult problems in gynecology.

The history is particularly important, and awareness of the high incidence of the lesion should be borne in mind. Endometriosis usually produces pain of one kind or another. Dysmenorrhea of the acquired type is of particular importance. Pyrexia associated with pain occurring at the time of the menses is important. Jeffcoat⁹ demonstrated that in 10 per cent of patients observed by him pyrexia was an important factor in making the diagnosis. This occurs during the menses, the temperature not ordinarily going above 102° F., and disappearing one to two days after the flow ceases. This might possibly confuse the differential diagnosis in ruling out pelvic inflammatory disease.

Ovulatory charts thus become of dual importance. The incidence of anovulatory menstruation in adenomyosis is particularly high. Spatt¹⁵ reported 72 per cent in carefully studied cases.

The history of previous abdominal operations becomes of increasing importance in light of the high incidence of endometriosis, in this series, among patients who had had operations. As shown in Table 7, 49 per cent of the 153 patients in the series had undergone previous abdominal operations, and 33 per cent had had operation involving incision of the genital tissue. These figures are almost in exact accord with those from the Mayo Clinic presented by Counseller.²

In Table 8 it will be noted that in the present series 15.7 per cent of cases were correctly diagnosed preoperatively. This contrasts with 6.8 per cent reported (ten years ago) by Fallas and Rosenblum.³ Perhaps this is encouraging, as it would tend to show that gradually physicians are becoming more cognizant of this condition. There were, however, only 38.6 per cent diagnosed at the surgical table, which is about in line, in this respect, with the figures reported by Fallas and Rosenblum. Perhaps this indicates that surgeons are not looking for or are not familiar with the gross lesion of endometriosis.

At present there is no specific hormonal index or guide available in establishing or indicating the diagnosis. There are a few instrumental aids in the diagnosis of pelvic endometriosis, namely:

1. The vaginal speculum, which may show the typical dark-bluish dome cyst becoming visible through the mucous membrane.
 2. The cystoscope, which is of aid in the diagnosis of vesical endometriosis.
 3. The culdoscope, which Te Linde has shown to be a potent aid in the hands of a competent observer.
- The proctoscope is of little aid in making a diagnosis of endometriosis involving the bowel.

TABLE 6.—*Involvement of Organs*

Organ	No. of Cases	Per Cent of Cases
Uterus	70	45.7
One ovary	63	41.2
Both ovaries	19	12.4
Pelvic peritoneum	27	17.8
Bladder	3	2.0
Sigmoid	7	4.6
Fallopian tube	5	3.3
Rectum	2	1.3
Small intestine	2	1.3
Round ligament	3	2.0
Uterosacral ligament	6	3.9
Cecum	1	.65
Infundibulopelvic ligament	2	1.3
Umbilicus	1	.65
Cervix	1	.65
Broad ligament	8	5.2

TABLE 7.—*Previous Abdominal Operations*

Type	No. of Patients	No. with Previous Laparotomy	Per Cent	No. with Genitals Incised	Per Cent
Internal	60	37	61.6	27	45.0
External	83	35	42.2	23	27.7
Combined	10	3	30.0	1	10.0
Total	153	75	49.0	51	33.3

TABLE 8.—*Record of Diagnosis in 153 Cases of Endometriosis*

	No.	Per Cent
Diagnosed preoperatively	20	13.1
Suspected preoperatively	4	2.6
Diagnosed at operation	52	34.0
Suspected at operation	7	4.6
Diagnosis by pathologist only	70	45.8

The finding, on physical examination, of rather firm, irregular, nodular, and "shotty" feeling tissue behind the cervix, which is unusually sensitive, in conjunction with the history remains one of the best clues to pelvic endometriosis. The nodules in the uterosacral ligaments can usually be best identified by rectal-vaginal examination. Where the lesion is more extensive, involving the ovaries and broad ligaments, a similar nodular process may be felt, often in conjunction with fixation, and a small cystic tumor may be palpated.

Fixed retroversion of the uterus should always arouse suspicion of endometriosis. Due to the lack of notation in case records no accurate data relative to the position of the uterus and associated endometriosis could be obtained. This is a serious error and might have been a factor in the failures of diagnosis noted in this report.

Testosterone may be used as an aid in the presumptive diagnosis of endometriosis. It will often suppress the symptoms with alleviation of pain and many times cause temporary regression of the palpable nodules and cysts. The author uses this reaction in conjunction with the history, examination, and other factors, to establish a diagnosis.

The diagnosis, then, rests on: (1) Carefully taken history; (2) Adequate and careful pelvic examination; (3) Visualization wherever possible, and biopsy of tissue; (4) Suppression of symptoms when testosterone is given.

As the recognition of endometrial implants in the peritoneal cavity is familiar to anyone now doing abdominal and pelvic operations, this apparently is not a problem. What is important, however, is the necessity of searching for the smaller implants, biopsy if they are found, and destruction of them when possible. This must be stressed, for although endometriosis is not always an advancing disease, it is usually so in the presence of active ovarian tissue. As endometriosis usually develops slowly, recognition of it, with determination by biopsy, is important with regard to the patient's future.

Another symptom of endometriosis which alone brings the patient to the physician for examination is relative or absolute sterility. In this series the records indicated that this was the primary problem in only 26 cases or 16.9 per cent, but in many cases it was an incidental observation. Of 143 married patients, 69 had reproduced and 74 had not (Table 9). These statistics are in agreement with many reports; Counseller² noted almost the same division.

TREATMENT

Those physicians who are most cognizant of the problems involved in complete castration of the female are in accord on at least one phase of the subject—namely, that ovarian conservation is necessary wherever possible. This is emphasized by Beecham,¹ Meigs,¹³ Counseller² and others. Castration in the female should be given as much consideration as castration in the male. Every attempt should be made to conserve the vital function of the ovary and its influence on emotional and physio-

logical balance. In this series, as can readily be seen, this factor was not given that consideration. In this respect there is little variance in these statistics with those presented in many other studies of the past. However, this is no excuse for continuation of ill-considered castration in the reproductive age groups.

As shown in Table 10, radical operations were done in 34 per cent of the 153 cases in the present series, a far higher figure than is justified in the light of present knowledge. There was a high incidence of radical operation in patients of all the age groups (Table 11), and it was particularly high in the younger patients for whom the most conservative of operations would seem to be indicated. For patients past the average age of menopause, the retention of ovarian tissue is not of great importance, and in the presence of extensive endometriotic lesions, complete oophorectomy should be done.

It is impossible at present to determine rules of procedure in the treatment of endometriosis. Perhaps nowhere in medicine is the judgment of the physician more taxed in determining the right answer relative to the patient's future well-being. In the presence of certain specific lesions, the answer may be more specific, depending entirely on the extent of the lesion. Often more than one organ is involved. In determining procedure in a specific case, the following points must be considered:

1. The degree of endometriosis present and the organs involved.
2. The age of the patient.
3. The desires of the patient relative to pregnancy, and also in regard to production of an artificial menopause. Many women who are given a complete understanding will gladly risk future operation or intensive glandular therapy rather than have castration immediately.
4. The emotional status of the patient.
5. Severity of the symptoms.
6. The need for immediate exploration. Often the diagnosis is not exact and the physician may be suddenly confronted with signs of obstruction, hemorrhage, possibilities of acute appendicitis, rupture of a viscus, twisted pedicle cyst, etc. In such circumstances there may be no question about the need for immediate operation. However, all the above points

TABLE 9.—Marital and Parity Status of Patients

	Internal Only	External Only	Combined	Total
Married (parous)	34	31	4	69
Married (nulliparous)	25	44	5	74
Unmarried	1	8	1	10

TABLE 10.—Type of Operation Employed

Type	No. Cases	Conserv.	Per Cent	Radical	Per Cent
Internal	60	40	66.6	20	33.3
External	83	56	67.4	27	32.6
Combined	10	5	50.0	5	50.0
Total.....153	101		66.0	52	33.9

TABLE 11.—Operations in the Various Age Groups

Age	Internal		External		Combined		Total			
	Conserv.	Radical	Conserv.	Radical	Conserv.	Radical	Conserv.	Per Cent	Rad.	Per Cent
20-24.....	0	0	6	1	0	0	6	85.7	1	14.3
25-29.....	0	1	13	0	0	0	13	92.8	1	7.2
30-34.....	0	1	16	6	0	0	16	69.6	7	30.4
35-39.....	10	4	11	4	0	3	21	65.6	11	34.4
40-44.....	9	2	8	11	3	0	20	60.6	13	39.4
45-49.....	9	6	1	5	1	0	11	50.0	11	50.0
50-54.....	10	2	1	0	1	1	12	80.0	3	20.0
55-59.....	1	3	0	0	0	1	1	20.0	4	80.0
60-64.....	1	1	0	0	0	0	1	50.0	1	50.0
Total.....	40	20	56	27	5	5	101	66.0	52	34.0

must be kept in mind when the actual lesion is determined to be endometriosis.

Simple endometrial cysts of the ovary often can be shelled out easily and the major portion of the functioning ovary preserved. This is done routinely by many physicians, including the author. It is no guarantee against further growth, but in many cases it is in itself sufficient.

Adenomyosis in women near the menopause is best treated by hysterectomy. In younger women, unless the lesion is of major extent, presacral sympathectomy will most often relieve severe dysmenorrhea. Presacral sympathectomy is of little value in endometriosis of the combined type, particularly if the pain is ovarian. If the infundibulopelvic ligament is resected, it may relieve ovarian pain but the blood supply of the ovary is seriously affected. If retroversion of the uterus is present in younger women, it is advisable to suspend the uterus in view of the high incidence of fixation and pain, dyspareunia, and further extension of the process into the rectovaginal septum.

Serious lesions of the bowel produced by endometriosis are not common. McGuff, Dockerty, Waugh and Randall¹² observed only 16 cases producing obstruction in 20 years' experience at the Mayo Clinic. In the present series, there were 12 cases involving the bowel, an incidence of 7.85 per cent. However, in none of these cases was the bowel obstructed. If symptoms of bowel obstruction arise, however, any patient regardless of age should be operated upon as soon as practicable. The type of operation depends on factors of age, involvement, and location of the lesion.

A phenomenon which has made a tremendous impression on the author is the regression of endometriosis during pregnancy. This has been observed by the author in every carefully followed case in his own practice, and it has been noted by other observers. In many of these cases there has been little regrowth, but in time the transplants ordinarily become reactivated unless further pregnancy intervenes. There is a tremendous bombardment of the endometrial implants by estrogen during this physiological amenorrhea which seems to have a depressing effect on the growth of the aberrant tissue.

In an attempt to produce a long period of amenorrhea, Karnaky¹⁰ has been treating patients with increasingly potent doses of diethyl stilbestrol. By this means, patients have been kept relatively amenorrheic for a period of several months. Karnaky reported almost complete regression of endometrial transplants in all patients so treated. This sounds feasible in view of the physiological results often associated with pregnancy, and if it is borne out in further experience it offers hope such as no other method to date can equal. Thus far the author has not had sufficient experience with this method to draw a conclusion, but patients being treated by this method are now under observation.

Hurxthal and Arnold⁷ reported that three patients with endometriosis were treated successfully with moderately large doses of diethyl stilbestrol.

They believed the basis of relief was suppression of progesterone. Misgivings were expressed regarding the long-term effect of estrogenic stimulation over a long period. Two of the patients were reported on after 18 and 24 months of continuous diethyl stilbestrol therapy.⁸ Endometrial biopsies indicated endometrium of hypoplastic type. As a result of these reports, this method of approach to the problem of endometriosis bears intensive study.

The use of testosterone in many cases offers a real aid in controlling the regrowth of ectopic endometrium following conservative operation. It should be kept in the armamentarium of the physician for use when necessary. Testosterone should also be kept in mind for use in controlling the symptoms of artificial menopause in younger patients who have been subjected to radical operation with castration and attending sequelae.

Greenblatt⁵ reported very successful results in experience with pellet implantations of testosterone, intramuscular testosterone propionate and methyl testosterone by mouth in the treatment of endometriosis. The author has had no experience with pellet implantations, but oral and intramuscular use has often given dramatic relief.

No trials of hormone therapy were reported in the case records of the patients studied in this series.

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CASE REPORTS

- ◀ Endocarditis Lenta Due to *Staphylococcus Aureus*
- ◀ Allergic Reaction to Decholin Used in Circulation Test
- ◀ Streptomycin in Tuberculous Meningitis with Emphasis on the Toxicity of Streptomycin

Endocarditis Lenta Due to *Staphylococcus Aureus*

Report of a Case

JAMES H. THOMPSON, M.D., San Francisco

THIS report of a single case of *staphylococcus aureus* endocarditis with penicillin treatment and clinical arrest is made in view of certain difficulties involved in the diagnosis and because of the mild afebrile course.

The only similar case found in the literature was one reported by MacNeal,² in which a patient with *staphylococcus aureus* endocarditis had low-grade fever, never over 100° F. except on one occasion after reaction to penicillin. In that case the patient had intermittent courses of treatment with penicillin over a period of several months. The amount of penicillin given, which was governed by the amount then (1944) available, ranged from 500 units to 10,000 units every two hours. The patient was finally "cured" when the article was published a year later.

In their section on bacterial endocarditis in "Oxford Medicine," Libman and Friedberg³ stated that "*staphylococcus aureus* has been reported as the cause of subacute bacterial endocarditis, but we have no confirmatory experience." They go on to discuss "mild cases of bacterial endocarditis," but they do not mention *staphylococcus aureus* as an etiological agent.

The patient in the present case had mild bacterial endocarditis. With regard to this case, however, "lenta" is considered a more exact word than "mild," because "lenta" implies a slow course. Before the advent of antibiotics, almost all bacterial endocarditis was fatal and it was difficult to convince members of a family that the patient had "mild endocarditis" when in the next breath it was explained that the outcome was likely to be fatal. On the other hand, it seems reasonable that "slow" endocarditis can terminate fatally.

CASE REPORT

A 72-year-old man was admitted to Franklin Hospital, San Francisco, on March 3, 1946, complaining of generalized arthralgia and weakness of one year's duration. He had been well until about one year before admission, at which time he noted the onset of "severe low-back pain" which had been attributed by a physician to a recent attack of "flu." The pain gradually increased and spread throughout the spine. About ten months prior to admission the patient began to lose weight, and the pain spread to the limbs. It became so severe that the patient was unable to dress himself.

About seven months prior to admission the hemoglobin value was found to be 60 per cent. Iron, liver extract, and

blood transfusions did not relieve the anemia. On admission to Franklin Hospital, the complaints were severe generalized pain in the back, made worse by motion, and severe pain in both arms, both shoulders, and both wrists. The pain was so severe as to interfere with sleep, and the patient was hardly able to get about his room. Any activity made the pain worse. There had been a loss of about 40 pounds in weight in ten months. The patient said he had not had chills or fever.

Past History: In childhood the patient had had Osgood-Schlatter disease. About 30 years before the present illness he had had "blood poisoning" of the left hand, followed by a "continuous siege of boils for several years." About 25 years ago "severely infected" tonsils had been removed, and this seemed to "cure the boils." Twenty years ago cholelithiasis had developed and cholecystectomy was done. About ten years ago the patient had noted angina pectoris on exertion and was told his blood pressure was "250." He had never noted edema or orthopnea, and he said that so far as he knew he had not had rheumatic fever. His first knowledge of cardiac murmur was about one year ago.

Physical Examination: The patient was well-developed but underweight. The general appearance was in accord with the stated age of 72. The patient was in extreme distress and did not seem comfortable in any position. There was a generalized *cafe au lait* tint to the skin, more pronounced over the chest. Several small pigmented moles were observed but no petechiae or other rash was noted. There was no apparent focus of infection. The chest was emphysematous with a few coarse, moist rales at both bases. The heart sounds were distant. A high-pitched, rough systolic murmur was heard over the whole precordium. This murmur was loudest at the apex and was transmitted to the axilla but not to the back. A soft, blowing systolic murmur was heard in the aortic area. The abdomen was slightly distended and tympanitic. The liver edge was 7 cm. below the right costal margin and was firm, smooth, and non-tender. The tip of the spleen was 4 cm. below the left costal margin; its edge was rounded, hard, and non-tender. The fingers were cyanotic and clubbed, but no splinter hemorrhages were seen. The reflexes were equal and active throughout. Otherwise, the physical examination was essentially normal.

Laboratory Work: There was a slight trace of albumin but no erythrocytes in the urine. The hemoglobin content in the blood was the equivalent of 10 gm. per 100 cc. Erythrocytes numbered 4,030,000 and leukocytes 6,200, with 60 per cent polymorphonuclear cells, 35 per cent lymphocytes, 4 per cent monocytes, and 1 per cent basophils. Results of Wassermann and Kahn tests were negative for syphilis. Total blood protein content was 8.21 gm. per 100 cc.

An electrocardiogram showed a pulse rate of 82, with normal rhythm and occasional premature beats; the P-R interval was 0.16 second; and the QRS interval was 0.08 second; T3 was diphasic.

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Blood cultures revealed the following: March 3, 1946: Positive for *staphylococcus aureus*.

March 7, 1946: Positive for *staphylococcus aureus*.

March 8, 1946: Positive for *staphylococcus aureus*. Plate count showed 25 colonies per cc. The organisms were sensitive to penicillin.

March 10, 1946: Positive for *staphylococcus aureus*.

March 15, 20, 25, and 30, 1946: Negative.

April 10, 20, and 30, 1946: Negative.

Treatment consisted of penicillin, 20,000 units every two hours, from March 10 to March 19, 1946. Then, from March 19 to April 17, 1946, 25,000 units was given every three hours. The total was 7,960,000 units in about five weeks.

Throughout a six-week stay in the hospital the patient was afebrile. The pulse rate ranged from 90 to 100 per minute, and respirations from 20 to 24 per minute.

By June 1946, three months after treatment was started, the patient had regained about two-thirds of the weight he had lost and was almost completely relieved of "arthritic pains." He had returned to his office where he worked several hours each day.

Now, three years later, the patient is working in his office ten to twelve hours daily. There has been no change in the cardiac murmur and no evidence of congestive failure. The "arthritic pains" are gone and blood cultures have shown no growths.

DISCUSSION

In this case an interesting problem of diagnosis was presented. The patient was seen in consultation primarily because of anemia which was believed to be the cause of

weakness. The enlarged spleen gave an important clue which, added to the findings of clubbed fingers, *cafe au lait* pigmentation, and cardiac murmur, caused endocarditis to be considered. It was surprising to find *staphylococcus aureus* as the offending organism, but repeated studies confirmed this finding. It is interesting to speculate as to the date of onset of septicemia, for it may well have started with the onset of the "arthritis" a year before. The fact that the "arthritic pains" ceased following treatment suggests that they were related to the septicemia. Afebrile *staphylococcus-aureus* septicemia of any duration is extremely rare. The relatively small doses of penicillin given appear to have been adequate. However, in light of recent experience, larger doses probably would be given now in similar circumstances.

SUMMARY

A case of afebrile *staphylococcus-aureus* endocarditis lenta with penicillin treatment and clinical arrest of three years is reported. Only one similar case has been reported in the literature. The importance of blood cultures, even in the absence of fever, is again demonstrated.

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Allergic Reaction to Decholin Used in Circulation Test

Report of a Case

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THE value of the circulation time as an aid in the determination of the presence of congestive heart failure has been well established.^{1,2} Decholin[®] (sodium dehydrocholate) was introduced into medicine for this purpose in 1931 by Winternitz.³ Other compounds such as calcium gluconate have been used for the same purpose but the latter has a synergistic action with digitalis and is potentially toxic when used in digitalized patients. Decholin, on the other hand, is relatively non-toxic and the only contraindications to its use as stated in a brochure prepared by the manufacturer* are: (1) obstructive jaundice, (2) bronchial asthma.

Untoward reactions to Decholin are rare. A search of the American literature reveals only a report by Norman⁴ in 1947 of three cases in which allergic reactions occurred subsequent to the injection of Decholin. In none of these cases was there a clear-cut history of previous allergic disease. In one case there was no reaction to the first injection of Decholin but a second injection one week later was followed by shock. In another case, injection was followed in one minute by a violent asthmatic attack. (In this instance, a review of the clinical findings suggests that the dyspnea was probably due to unrecognized asthmatic bronchitis.) In the third case, widespread diffuse urticaria developed five minutes after the injection of Decholin.

The following case report is submitted as the fourth case in which frank allergic manifestations occurred following the parenteral use of Decholin.

* Ames, Inc., Elkhart, Ind.

CASE REPORT

The patient, a 52-year-old white woman, was first observed April 12, 1949, for evaluation of hemoptysis. X-ray films of the chest made at this time revealed healed apical pulmonary tuberculosis ("fibrocalcific scarring but no evidence of active parenchymal disease"), bilateral basal bronchiectasis, and generalized pulmonary emphysema. A study of the sputa on several occasions did not reveal Koch's bacilli. There had been previous attacks of hemoptysis in 1918, 1938, and 1942. There was no record of previous allergic manifestation. In 1942 the patient had had a "heart attack," characterized by substernal oppression in the xiphoid area and pain along the left anterior costal margin with pronounced tachycardia. Electrocardiograms made during this attack were not available but an electrocardiogram made during the present study revealed a left bundle branch block. Slight left ventricular enlargement was noted in an x-ray film of the chest. The amount of bloody sputum decreased sharply during a six-day stay in the hospital, and the patient was discharged April 18, 1949.

In order to decrease the amount of purulent sputum, inhalations of penicillin dust were taken at home, but after several days a local sensitization developed in the form of a sore throat.

On May 16, 1949, the patient complained of dyspnea on recumbency, together with headache. Both symptoms were relieved only by sitting up repeatedly during the night. Physical examination revealed the lungs to be clear. The heart findings included a soft systolic murmur which was Grade 2 at the apex and was transmitted to the axilla. The systolic murmur was Grade 1 at the base. The rhythm was regular. The blood pressure was 155 mm. of mercury systolic and 95 mm. diastolic. The liver was not enlarged. No edema of the lower extremities was discernible nor was there visible distention of the peripheral veins of the extremities.

Because of the symptoms of left ventricular failure, it was decided to determine the circulation time, and 3.0 cc. of Decholin (sodium dehydrocholate 20 per cent solution) was injected into the antecubital vein of the left arm. The circulation time was found to be 15 seconds. Five minutes later the patient began to complain of a strange sensation on the anterior chest wall. Examination revealed pronounced erythema of the upper anterior chest wall and flushing of the face. Soon afterward wheals typical of urticaria appeared in the erythematous area of the chest, and the patient complained of itching. A few moist rales were noted in the bases of both lungs. Hypodermic injection of two minims of epinephrine hydrochloride 1:1,000 and the oral administration of 50 mg. of pyribenzamine abated the symptoms. There were no sequelae to this attack.

DISCUSSION

The case herein reported corresponds, in character of allergic manifestations, with one of the cases reported by Norman.³ In neither case was there history of allergic reaction, but the patient in the case herein reported had allergic response to penicillin dust a few weeks before Decholin was given. Allergic sensitivity to drugs, whether given orally or parenterally, has long been observed. It has been noted with respect to heavy metal salts such as arsenic, mercury, bismuth and gold, such synthetic compounds as acetylsalicylic acid, aminopyrine and barbiturates, and tissue extracts such as insulin and liver extract. The explanation of allergic reaction to drugs was recently summarized by

Feinberg,¹ who stated that: "The simple chemical substance per se is incapable of acting as an antigen, but in combination with body substances, particularly proteins, it becomes a perfect antigen capable of producing the allergic manifestation. This concept explains the failure of most drugs to cause skin test reactions and explains the absence of circulatory antibodies."

SUMMARY

Allergic manifestations in the form of urticaria and erythema were noted in a patient who was given Decholin® parenterally to determine circulation time. Only three such cases have been reported previously.

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Streptomycin in Tuberculous Meningitis with Emphasis on the Toxicity of Streptomycin

Report of a Case

DANIEL J. VRACIN, M.D., Downey

ON March 27, 1947, a four-year-old white girl was admitted to Duke Hospital (Durham, N. C.) with a history of convulsions, fever, and vomiting of 16 days' duration.

History: When the child was one and one-half years old the parents noted that she held her back rather rigid. She walked with short, mincing steps, and had a moderate amount of difficulty in getting off the floor. The child was very irritable. She frequently cried out when asleep, and perspired profusely at night. A spinal deformity became noticeable in September 1946. Roentgenograms revealed necrosis of the ninth and tenth thoracic vertebrae. A diagnosis of Potts' disease was made. A nursemaid who had cared for the child most of her life was found to have pulmonary tuberculosis. The patient underwent a spinal fusion of the ninth, tenth, and eleventh thoracic vertebrae in October 1946.

March 11, 1947, the patient had fever and complained of headache and nausea. She vomited frequently and became delirious. March 18 she had a generalized convulsion lasting four hours. The following day the only residual effect was ptosis of the right eyelid. Streptomycin (150 mg. every three hours) was given for eight days, and the patient was then transferred to Duke Hospital for further study and treatment.

The patient, who appeared to be well nourished, was apathetic and seemed to be chronically ill. The temperature was 38.5° C.; pulse rate was 104; respirations were 28 per minute; blood pressure was 104 mm. of mercury systolic and 80 mm. diastolic. Hearing was intact. The external auditory canals were clear, the tympanic membranes were intact, and there was no evidence of middle ear infection. There was ptosis of the right upper eyelid. The right pupil was larger than the left; both reacted to light and accommoda-

tion. Fundoscopic examination revealed blurring of both optic discs. The extraocular movements were performed without difficulty. There was slight nuchal rigidity. Chest examination was negative. The abdomen was soft and no organs or masses were palpable. Neither Babinski's nor Kernig's sign was unequivocally present. The tendon reflexes were hypoactive. The superficial reflexes were present. There was no localized muscular weakness and no paralysis.

Leukocytes in the blood numbered 10,300 per cu. mm. with normal differential of cells. Hemoglobin content was 13.2 gm. per 100 cc. The urine was normal and results of serologic tests were negative. There were 123 cells in the clear spinal fluid, with mononuclear cells predominant. Reaction to a Pandy's test was 1+. No organisms were found on smear of the fluid and no pellicle formed in 24 hours. Routine and tuberculin cultures showed no growth. Spinal fluid proteins were 142 mg. per 100 cc.; chlorides 680 mg. per 100 cc.; and dextrose 40 mg. per 100 cc. Reaction to tuberculin skin test was positive 1:10,000. The Weltmann coagulation reaction was zero. Roentgenograms of the lungs were read as normal. The films of the vertebral column showed loss of calcium. There was evidence of destruction of the ninth, tenth, and eleventh thoracic vertebrae without paravertebral swelling. Films of the skull were normal.

The diagnosis was tuberculous meningitis.

Intensive streptomycin therapy was given over a period of 38 days. A total of 3.20 gm. was given intrathecally, and 80.95 gm. intramuscularly. The intramuscular dose was 350 mg. every three hours. The patient complained of pain and tenderness at the sites of injection. The intrathecal dose was started at 50 mg. and increased slowly to 200 mg. This dose was not tolerated. The patient became delirious and vomited. Nystagmus and vertigo were evident. The dosage was lowered to 100 mg. for the duration of the therapy. On the 20th day of treatment the patient had a generalized clonic convolution. She had five such episodes during the next four days. The fever persisted during the entire course of treatment. On the 32nd day of therapy the intramuscular streptomycin was discontinued and the convulsions stopped. When

TABLE I.

- A. Local reactions: (1) irritation, (2) paresthesia.
- B. Neurological manifestations: (1) headache, (2) nausea and vomiting, (3) somnolence, (4) nystagmus, (5) vertigo, (6) tinnitus, (7) ataxia, (8) partial or complete deafness, (9) increase in spinal fluid cell count.
- C. Allergic reactions: (1) urticaria with or without pruritus, (2) fever, (3) purpura, (4) skin eruptions, (5) nausea and vomiting, (6) eosinophilia, (7) leukopenia.
- D. Kidney: (1) cylindruria, (2) casts (granular, hyaline, cellular), (3) albuminuria, (4) hematuria, (5) urinary retention.
- E. Miscellaneous: (1) hypotension, (2) synovitis.

treatment was resumed on the 36th day, the convulsions returned accompanied by a maculopapular eruption. With final cessation of therapy, the rash disappeared, and there was no recurrence of convulsions. The patient became more rational and began taking an interest in toys. Examination at that time revealed impaired hearing. During the next four days the deafness became complete.

On the 53rd hospital day the patient, then in excellent condition, was discharged to the care of the family physician.

Two years after discharge the family physician reported that the patient was getting along nicely and her activity was normal for a child of her age. However, the deafness was still present.

DISCUSSION

Since the discovery of streptomycin in 1944, there have been numerous reports on its toxicity. It is difficult to ascertain how much of the reactions are caused by impurities and how much by streptomycin alone.

Table 1 is a list of toxic manifestations that was made up from reports in the recent literature.

In this case report, the convulsions that occurred during the course of therapy are attributed to the streptomycin. This was proven when the drug was discontinued and the convulsions ceased. With the resumption of therapy, the convulsions recurred. In this case the manifestations of toxic reaction encountered were fever, local irritation, maculo-

papular rash, lethargy, coma, convulsions, vertigo, nystagmus, complete deafness, nausea and vomiting, and eosinophilia.

Leary Clinic.

SUMMARY

Successful treatment of tuberculous meningitis with streptomycin is reported.

The toxic manifestations reported in the literature have been listed.

Symptoms of intoxication noted in the case reported are discussed.

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California MEDICINE

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EDITORIALS

The World Medical Association

Observers of international medical practice and students of medical economics have noted with considerable pleasure the operations of the World Medical Association. Formed in 1947, the W.M.A. consists of the national medical associations in 40 countries and expects to reach a total membership of 60 countries through new admissions.

Here is a truly professional organization of physicians, unlike the World Health Organization and UNESCO, which are supported by government funds as parts of the United Nations. The World Medical Association is supported by contributions from the medical associations in the various member nations and from individual physicians and allied organizations and other groups in these countries. It receives no governmental support and has no governmental or political strings attached to its activities and pronouncements.

Best assay of the World Medical Association comes in its own statement of its objectives, which are listed as:

1. To promote closer ties among national medical associations and doctors.
2. To maintain the honor and protect the interests of the medical profession.
3. To study and report on professional problems.
4. To organize an exchange of information on matters of interest to the medical profession.
5. To present the world medical opinion to W.H.O. and UNESCO.
6. To assist all people of the world to attain the highest possible level of health.
7. To promote world peace.

In pursuit of these objectives, the World Medical Association has instituted several studies which are now under way. These cover such subjects as the status of the medical profession of the world, the status of world medical education, postgraduate medical education and specialist training, medical advertising and nostrums, a survey of cult practice and an international code of medical ethics. These are the studies which can best be carried on by the doctors themselves, not by governmental representatives in W.H.O., who are primarily interested in public health matters. Perhaps the most significant of W.M.A.'s studies is a continuing review and summary of social security developments throughout the world with particular reference to plans of medical care.

As a young organization, W.M.A. has attracted an unusually high degree of interest and attention. Part of this springs, no doubt, from the broad fields of endeavor hinted at in the list of studies under way; possibly an even larger part comes from the very nature of the organization itself, an international federation of physicians and their own national societies. For the first time, the practicing physicians of the world can meet in an organization of their own, free of political domination, to discuss and seek solutions to international problems of mutual interest.

The American Medical Association has played an active part in the development of W.M.A. and has been honored by the election of Dr. Louis A. Bauer of New York as secretary of the association. In turn, California has been honored by the appointment of Dr. John W. Cline as one of the A.M.A. delegates

to W.M.A. International headquarters are maintained in New York.

As against such an auspicious beginning and such an inspiring list of objectives and studies, it is unfortunate that W.M.A. has found financial difficulties besetting it. The constituent associations are more than willing to contribute their fair share of funds to run the organization but most of them find themselves up against national currency restrictions which prohibit their sending dollars out of their own national boundaries. The medical association in Great Britain, for instance, could not send dollars to this country as dues to W.M.A., but it could and did contribute by meeting the expenses of the November 1949 meeting in London.

Inasmuch as the United States remains the only major nation without international currency restrictions, it is incumbent on this country at present to supply the modest financing required by W.M.A. A national committee has been established for this purpose in New York and has announced as its objective the securing of 5,000 American physicians as individual members at ten dollars each per year.

Such a membership would achieve the financial goal of W.M.A. and eliminate the need of soliciting funds from state and county medical societies, pharmaceutical producers, allied professional organizations and others.

CALIFORNIA MEDICINE is not a fund-raising publication, but in the matter of W.M.A. it may with propriety express an attitude. Here is an organization so worthy of medical support that any support this publication can give it is gladly extended. California doctors are noteworthy for their support of sound causes in the interest of medicine and it is hoped they may accept this challenge in their customary manner of generosity. Memberships for individual physicians carry with them a subscription to the publications of W.M.A. and other valuable returns.

Membership dues may be sent direct to the World Medical Association, United States Committee, at 2 East 103rd Street, New York 29, or through the office of the California Medical Association. The cause is right, the hour ripe.

Letters to the Editor . . .

Tuberculin "Activator"

In 1927 it was shown by Rich and Lewis³ that living tissue cultures of leukocytes from tuberculous guinea pigs are hypersensitive to tuberculin. Favour¹ and his associates of Harvard University afterwards demonstrated the same tuberculin hypersensitivity in the leukocytes of tuberculous patients. When suspended in normal human plasma, such leukocytes undergo fairly rapid lysis on the addition of a small amount of old tuberculin. Leukocytes from normal tuberculin-negative individuals, similarly suspended, resist lysis. Since lysis takes place in the presence of normal plasma, Favour concluded that it is an example of purely cellular rather than humoral allergy.

This conclusion was subsequently challenged by Miller,² based on his belief that the earlier tests were performed with inadequately washed leukocytes. White cells obtained from the bloods of tuberculous patients were therefore repeatedly washed in isotonic salt solution. Duplicate samples were suspended in normal human plasma and in the plasmas of tuberculous individuals. Control tests were made with the leukocytes of normal tuberculin-negative individuals.

To 0.4 cc. of such cell suspensions 0.1 cc. of dilute tuberculin was added. Total white cell counts were made immediately and after 60 minutes' in-

cubation at 37° C. Within the limits of the experimental error no reduction in initial cell count was noted in any of the leukocytes suspended in normal tuberculin-negative plasma. Leukocytes from both normal individuals and from tuberculous patients, however, underwent from 20 to 35 per cent reduction in cell count in all tubes in which they were suspended in plasma from tuberculous individuals.

Tuberculin cytology thus occurs only in the presence of tuberculous serum, both normal and tuberculous leukocytes being equally susceptible to this lysis. Lysis is thus due to the adjuvant action of some specific component of tuberculous plasma. This component is non-dialyzable and is inactivated by heating to 56° C. for 15 minutes. It is precipitated with the globulin fraction of the plasma proteins.

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CALIFORNIA MEDICAL ASSOCIATION

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NOTICES AND REPORTS

Public Funds for Hospital Construction

Within the past few years both federal and state "gifts" have become available for the construction of hospital facilities. Conditions are attached to the receipt of such funds, and legal restrictions are applicable in the granting and use of this type of public subsidy.

The California Medical Association deems it advisable to review the subject of federal or state funds for hospital construction and to express certain principles which the Association submits should be observed by any organization or body considering the use of such funds for the construction of hospital facilities.

The following facts in regard to federal and state funds are applicable at this time, and it is upon these facts that the principles enunciated herein are based.

1. Federal funds for the 1950-1951 fiscal year available for California hospitals amount to about \$5,000,000.

2. State funds available for the 1949-1950 fiscal year amount to \$2,000,000. Under state law this amount may be raised to match federal funds.

3. Federal funds are allocated only after approval of the hospital construction project by the California State Department of Public Health; these funds are available to state, county, municipal or voluntary (non-profit) hospitals.

4. State funds are available only to state, county or district hospitals; a state constitutional provision prohibits the allocation of such state funds to any private institution.

5. Federal funds are available only to those hospitals whose applications have been approved by the State Department of Public Health, in accordance with a master hospital plan developed by that department for the entire state and in accordance with other regulations established for the screening of applications for funds.

6. Applications already received by the State Department of Public Health total about \$100,000,000. This sum indicates that a long waiting period lies ahead of any successful applicant for state and/or federal funds in view of approximately \$7,000,000 present annual total available.

7. The allocation of federal funds carries with it the observance of various restrictions, including construction requirements, availability of hospital facilities for all classes of people, and others.

8. The use of state and/or federal funds immediately opens the door to substandard practitioners who claim that the public funds allocated to the hospital constitute a public trust and who demand that they be admitted to the staff of the hospital, regardless of professional status or skill.

9. Opening of hospital staffs to substandard practitioners makes it impossible for such hospitals to maintain recognized internships, residencies or nursing schools. The lack of these services deprives the patient of the best possible care.

10. In the case of "district hospitals" the observance of state legislation relative to professional staff appointments is required. Such legislation now permits practitioners other than licensed doctors of medicine to serve on staffs of "district hospitals." Additional legislation providing an even broader basis of staff membership could be adopted at any future legislative session. In some areas, due to small or scattered population or other definite factors, resort to the "district" method of ownership may be necessary.

In view of these elements, the California Medical Association, acting through its Council, asserts its belief in the following principles, which are offered as a guide to physicians and

others who are seeking means of raising funds for hospital construction:

1. The care of the patient is the chief consideration in the building and maintenance of hospitals and the best possible care cannot possibly be given where governmental restrictions or requirements make it impossible to provide services which would otherwise be available for the good of the patient.

2. The use of state or federal funds for construction of either private or public hospitals should be discouraged. After construction, maintenance costs are continuous and can only be assured through local community support.

3. Funds for hospital construction should be raised by private subscription, by endowment or by other means which are available and which will not entail building, staff or other

restrictions which operate against the good of the patient or which unduly increase the cost of construction. If hospital beds are needed in any community, a real need should be demonstrated to the citizens of the community, who in turn should respond with contributions to a community fund. The experience in Kansas proves that this method is practical.

4. In some areas where a definite need for hospital beds has been demonstrated and where community resources are insufficient to meet the cost of construction, it is recognized that public funds may need to be employed. However, such instances should be few in number and should be most carefully examined to determine the true facts of (1) need, (2) capacity to raise funds by non-governmental means, and (3) ability to maintain and operate after construction.

Change in A. M. A. By-Laws—Membership Dues

To the Secretaries of the Constituent State and Territorial Medical Associations:

The House of Delegates of the American Medical Association at its meeting in Washington, D. C., December 6 to 8, 1949, adopted amendments to the By-Laws of the American Medical Association whereby Division One, Chapter II, Tenure of Membership, has been changed to read as follows:

CHAPTER II

Tenure and Obligations of Membership; Dues

Section 1.—When the Secretary is officially informed that a member is not in good standing in his component society he shall remove the name of said member from the membership roll. A member shall hold his membership through the constituent association in the jurisdiction of which he practices. Should he remove his practice to another jurisdiction, he shall apply for membership through the constituent association in the jurisdiction to which he has moved his practice. Unless he has transferred his membership within six months after such change of practice, the Secretary shall remove his name from the roster of members.

Section 2.—Annual dues, not to exceed \$25.00, may be prescribed for the ensuing calendar year in an amount recommended by the Board of Trustees and approved by the House of Delegates. Each active member shall pay said annual dues to his constituent association for transmittal to the Secretary of the American Medical Association.

An active member who is delinquent in the payment of such dues for one year shall forfeit his active membership in the American Medical Association if he fails to pay the delinquent dues within thirty days after notice of his delinquency has been mailed by the Secretary of the American Medical Association to his last known address.

Any former member who has forfeited his membership because of being delinquent in payment of dues may be reinstated on payment of his indebtedness.

You will note that the following important changes have been made:

(A) The word "Dues" has been added to the title of Chapter II.

(B) Chapter II has been divided into two sections.

(C) The first sentence of Chapter II, which read, "Membership in this Association shall continue as long as a physician is a member of a component society of the constituent association through which he holds membership," has been deleted.

(D) The words "of the American Medical Association" have been added after the word "Secretary" where clarification is necessary.

(E) The sentence, "An active member shall pay dues or assessments as may be prescribed by the Constitution or By-Laws," has been deleted.

(F) The words "in the American Medical Association" have been added after the words "shall forfeit his active membership" in the second paragraph of Section 2.

(G) The sentence forming the third paragraph of Section 2, with regard to reinstatement, is a new addition to Chapter II.

(H) A new paragraph, forming the first paragraph of Section 2, providing for annual dues not to exceed \$25.00 has been added to Chapter II.

The House of Delegates, on recommendation of the Board of Trustees, set the membership dues for the year 1950 at \$25.00.

The full effect of the new provisions will have to be studied and developed during the next year. However, the following interpretations of the amended By-Laws are offered for your guidance at this time:

(a) Active membership in the American Medical Association will continue to be limited to those members of constituent associations who (1) hold the degree of Doctor of Medicine or Bachelor of Medicine, and (2) are entitled to exercise the rights of active membership in their constituent associations as provided in Article 5 of the Constitution of the American Medical Association.

(b) A member of the American Medical Association shall lose his membership in the Association when the Secretary

of the American Medical Association is officially informed that a member is not in good standing in his component society or is delinquent in the payment of the American Medical Association dues established by the above change in the By-Laws.

(c) Forfeiture of membership in the American Medical Association due to failure to pay dues will have no effect on membership in the component or constituent medical societies unless the component or constituent societies amend their respective constitutions and by-laws. It is, therefore, possible that a physician may be a member of his component and constituent societies and at the same time not be a member of the American Medical Association.

(d) The amended By-Laws provide for the collection of the American Medical Association membership dues by the constituent associations for transmittal to the Secretary of the American Medical Association. The detailed method to be adopted by each constituent association will vary in each state. In general, the method utilized by each state for the collection of its own component and constituent association dues should be followed.

Some of the problems involved in the collection and transmittal of dues will be considered in a later communication to you.

It is planned to provide each member of the American Medical Association a membership card and certificate of membership when his dues are paid.

It will be necessary for the Secretary of the American Medical Association to notify those members who are delinquent in the payment of their dues, and this office will, therefore, require a complete list of all active dues paying members.

No changes have been made in the Constitution and By-Laws of the American Medical Association with respect to Fellowship. Eligibility for Fellowship and annual Fellowship dues of \$12.00 remain the same. Under the present By-Laws a Fellow will pay for the year 1950 total membership and Fellowship dues of \$37.00.

The following members may be exempted from the payment of the \$25.00 American Medical Association membership dues: retired members; members who are physically disabled; interns, and those members for whom the payment of such dues would constitute a financial hardship.

No member should be exempted from the payment of his American Medical Association dues who is not exempted from his component and constituent society dues.

**GEORGE F. LULL, M.D.
Secretary and General Manager
American Medical Association**

Industrial Fee Schedule

Following many months of conferences, the Executive Committee of the California Medical Association has reached an agreement with the compensation insurance carriers on a schedule of fees for industrial injury cases. This schedule has been presented to the Industrial Accident Commission of the State of California, which scheduled a hearing on the proposed fee schedule for February 6, 1950.

The Council has approved and ratified the actions of the Executive Committee, a fact of which the Industrial Accident Commission has been notified.

Included in the agreement with the insurance carriers is the establishment of a continuing joint committee of the Association and the carriers, for the dual purpose of making a continuing study of the fee schedule, with a view toward periodic revisions, and of looking into alleged abuses of the industrial accident provisions by either insurance carriers or physicians. The Association's committee for this purpose will be named by the Council, the insurance committee by the carriers. Thus, for the first time since the industrial accident laws went into effect, 38 years ago, there is a continuing liaison between carriers and doctors. Much good should come from this arrangement.

As soon as the Industrial Accident Commission rules on the proposed fee schedule, the Association plans to send copies to all members.

New Postgraduate Seminar Director

Dr. C. A. Broaddus of Stockton has been appointed director of postgraduate seminars for the Committee on Postgraduate Activities, to succeed Dr. Carroll B. Andrews of Sonoma who resigned effective February 1 because of limited time available for duties outside his own practice.

The Council accepted the resignation with regret and expressed appreciation for the valuable services rendered by Dr. Andrews. He had been serving on a half-time basis since January 1948, and in that time had arranged 18 seminars throughout the state.

Dr. Broaddus, who will serve on a half-time basis with compensation of \$500 a month, was appointed by the Council upon proposal by Dr. John Riddock, chairman of the Committee on Postgraduate Activities.

The new director of seminars, a graduate of Western Reserve University Medical College and a practicing physician in Stockton since 1924, has a background of experience in arranging postgraduate programs. He was president of the San Joaquin County Medical Society in 1935 when the Stockton Postgraduate Study Club was formed and has been chairman of the club for several years. In this capacity he has been successful in bringing outstanding authorities to Stockton to address the club, which presents evening courses monthly except during the summer months. Meetings have been well attended not only by Stockton physicians but by physicians from other towns in San Joaquin and surrounding counties.

Brochure on Medical Economics

Plans are going forward for publication by the California Medical Association of a bi-monthly brochure on medical economics to be circulated among medical students, interns and resident physicians in California.

Principal purpose of the publication, plans for which have been approved by the C.M.A. Council, is to "prepare interns, residents and medical students for membership in the medical community and, more specifically, in the California Medical Association."

According to a prospectus drawn up by a special committee which was named by the President of the C.M.A. at the direction of the House of Delegates to study the matter, this will be done by publishing in the proposed brochure:

"1. Editorial and news material designed to properly indoctrinate these men in the principles of free enterprise in which we believe.

"2. Factual material concerning the economics and technique of medical practice.

"3. Light news and gossip of interest to medical students, interns and residents.

"4. An open forum in which the medical students, interns and residents may express themselves."

The committee has recommended that initially the brochure be made up of four 8½ by 11-inch pages. No date for the first issue has been set as yet.

The members of the committee which made the recommendations with regard to the brochure are: Drs. J. Lafe Ludwig, chairman, Los Angeles; Russell Lee, Palo Alto; John Graves, San Francisco; Robert Haining, Glendale; and Justin Stein, Los Angeles.

In Memoriam

BRAMBLE, EARL G. Died in December 1949, aged 33, in an airplane accident near Banning, California. Graduate of the University of Kansas School of Medicine, Lawrence-Kansas City, 1941. Licensed in California in 1946. Dr. Bramble was a member of the Orange County Medical Society, the California Medical Association, and the American Medical Association.

BURTON, JAMES WILLOUGHBY. Died in Van Nuys, December 20, 1949, aged 40. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1938. Licensed in California in 1938. Dr. Burton was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

DURR, SAMUEL ABRAHAM. Died in San Diego, December 4, 1949, aged 55, of a heart ailment. Graduate of Northwestern University Medical School, Chicago, 1918. Licensed in California in 1920. Dr. Durr was a retired member of the San Diego County Medical Society, and the California Medical Association.

FROHMAN, BERTRAND SYDNEY. Died in December 1949, aged 55. Graduate of the College of Physicians and Surgeons of San Francisco, 1920. Licensed in California in 1920. Dr. Frohman was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

GLOOR, EUGENE EDWIN. Died in Salinas, March 18, 1949, aged 52. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1923. Licensed in California in 1923. Dr. Gloor was a member of the Santa Cruz County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

GOLDBERG, ALBERT TOBIAS. Died in Fresno, December 20, 1949, aged 43, of a coronary occlusion. Graduate of the College of Physicians and Surgeons, Los Angeles, 1921. Licensed in California in 1921. Dr. Goldberg was a member of the Fresno County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

JENNINGS, ALFRED NORMAN. Died in San Bernardino, November 30, 1949, aged 46, after an extended illness. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1935. Licensed in California in 1935. Dr. Jennings was a member of the San Bernardino County Medical Society, the California Medical Association, and the American Medical Association.

JOHNSTONE, WILLIAM ARTHUR. Died in Glendale, December 8, 1949, aged 56. Graduate of the College of Medical Evangelists, 1924. Licensed in California in 1924. Dr. Johnstone was a member of the Kings County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

MCGARVEY, HARRY. Died in Atascadero, November 18, 1949, aged 75. Graduate of Western Reserve University School of Medicine, Cleveland, 1897. Licensed in California in 1914. Dr. McGarvey was a member of the San Luis Obispo County Medical Society, the California Medical Association, and the American Medical Association.

MARKS, SELBY HAROLD. Died in Pittsburg, December 14, 1949, aged 59, of polycythemia vera. Graduate of the University of California Medical School, Berkeley-San Francisco, 1913. Licensed in California in 1913. Dr. Marks was a member of the Contra Costa County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

MILLER, GEORGE HERBERT. Died in Sherman Oaks, December 20, 1949, aged 70. Graduate of McGill University Faculty of Medicine, Montreal, 1901. Licensed in California in 1923. Dr. Miller was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

SCHUSTER, EMILE GABRIEL. Died in Oakland, December 23, 1949, aged 44, of coronary thrombosis. Graduate of McGill University Faculty of Medicine, Montreal, 1940. Dr. Schuster was a member of the Alameda County Medical Association, the California Medical Association, and the American Medical Association.

WOOD, FREDERICK WEBSTER. Died in Alhamhra, December 20, 1949, aged 75, of a heart attack. Graduate of the Hahnemann Medical College and Hospital, Chicago, 1899. Licensed in California in 1920. Dr. Wood was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

Dr. Paul E. Dolan of Livermore was elected president of the Southern Branch of the Alameda County Medical Society at a recent meeting, succeeding Dr. H. C. Crockett of Hayward. Dr. T. A. Runyon of Castro Valley was elected secretary. The branch society, which was formed two years ago, is a part of the Alameda County Medical Society.

FRESNO

Dr. Clarmont P. Doane of Fresno was elected president of the Fresno County Medical Society at the annual meeting held in December. He succeeds Dr. William L. Adams, Jr. Others elected were: Dr. Hugh Awtry, president-elect; Dr. Kendall B. Holmes, vice-president; Dr. Fred E. Cooley, treasurer; Drs. Neil J. Dau, J. E. Young and Henry A. Randel, delegates to the California Medical Association.

LOS ANGELES

Dr. Harold E. Pearson has been appointed head of the department of public health and preventive medicine in the University of Southern California School of Medicine. Dr. Pearson had been a member of the department of microbiology at U.S.C. since 1944.

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Dr. William J. Matousek of Glendale recently was honored as the city's "physician of the year" by the Glendale Branch of the Los Angeles County Medical Association. Dr. Ted S. Kimball, newly elected president of the Glendale Branch, presented Dr. Matousek with a plaque inscribed: "In appreciation of his work as a physician who has contributed most to the advancement of the medical profession of Glendale in the year 1949."

Other officers of the Glendale Branch for 1950 are Dr. Gerald Beck, vice-president, and Dr. Chester Roberts, secretary-treasurer.

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Dr. Chester Alcorn has been elected president of the Pomona Valley Branch of the Los Angeles County Medical Association for 1950, and Dr. Edward J. Mueller, Jr., secretary-treasurer.

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California Physicians Service recently opened an account at the California Bank in Los Angeles to handle all payments for physician-members in Southern California. The greatly increased number of C.P.S. physician and beneficiary members in Southern California made possible expansion of the Los Angeles staff to handle payments directly for physicians in that area, rather than through San Francisco as in the past.

ORANGE

Officers of the Orange County Medical Association for 1950, elected at a meeting in December are: President, Dr. Ardath H. Wightman of Laguna Beach; Dr. C. Emmett Raitt, Santa Ana, vice-president; Llewellyn E. Wilson, Anaheim, secretary-treasurer. Elected as delegates to the California Medical Association were Dr. A. Norton Donaldson of Santa Ana, Dr. Charles E. Irvin, Anaheim, and Dr. G. Wendell Olson, Fullerton.

RIVERSIDE

Dr. Philip Corr of Riverside was installed as president of the Riverside County Medical Association for 1950 at a recent dinner meeting which was presided over by Dr. H. M. F. Behnemann, outgoing president. Dr. H. H. Martin became vice-president of the organization, and Dr. Cecil Lloyd, who was reelected, was installed as secretary-treasurer.

Dr. R. Stanley Kneeshaw, president of the California Medical Association, and **Dr. Dwight Murray**, a trustee of the American Medical Association, were guests at the meeting. Both spoke on the political drive for socialization of medicine and its effect on medical practice.

SAN MATEO

Dr. Harold Marks resigned January 15 as superintendent of the San Mateo Community Hospital and has taken a similar position at San Joaquin County Hospital. In his new post he succeeds Dr. John Smiley, who resigned.

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Plans are reported under way in San Mateo County for a drive for public subscription to a fund for a larger and more modern **San Mateo County Blood Bank**. Dr. Carl Hoag, president of the blood bank, reported recently that the bank must vacate its present quarters on property of the San Mateo School Department. The blood bank owns a building site in San Mateo but must raise money for construction.

YUBA-SUTTER-COLUSA

Dr. Stanley R. Parkinson of Marysville has been elected president of the Yuba-Sutter-Colusa Medical Society, succeeding Dr. Anthony Fratis, also of Marysville.

GENERAL

Organizing so that they may bring coordinated effort to bear on solutions of areawide problems of public health, county health officers of eight San Joaquin counties have formed the **San Joaquin Valley Health Officers' Association**. The counties embraced in the new organization, and the names of representatives, follow: Merced, Dr. C. A. Moyle; Tulare, Dr. R. Lynn Knight; Madera, Dr. J. T. Deuel; Fresno, Dr. William F. Stein; Kern, Dr. William C. Buss; Kings, Dr. Donald E. Upp; Stanislaus, Dr. George O'Brien; San Joaquin, Dr. E. M. Bingham.

At the first meeting of the association, Dr. Moyle was elected president, Dr. Knight vice-president, and Dr. Deuel secretary.

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The annual meeting of the **American Goiter Association** will be held in the Shamrock Hotel, Houston, Texas, March 9, 10 and 11.

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During March, volunteers in communities throughout the nation will ask the American people to contribute \$67,000.00 to carry on the services of the **American Red Cross** for the 1950-51 fiscal year. The goal for California is \$6,700,000.

POSTGRADUATE EDUCATION NOTICES

College of Medical Evangelists, Graduate School of Medicine

Course: Histology and Histopathology of the Eye (50 hours).

Date: March 1 to June 21, 1950, Wednesdays 7:00 to 10:00 p.m.

Fee: \$75.00.

Course: Varicose Veins (6 periods).

Date: March 3 to April 6, 1950, Thursdays 7:00 to 9:00 p.m.

Fee: \$25.00.

Course: Endocrinology (8 periods).

Date: April 3 to May 22, 1950, Mondays 8:00 to 9:30 p.m.

Fee: \$30.00.

Course: Minor Orthopedic Surgery (8 periods).

Date: April 6 to May 25, 1950, Thursdays 8:00 to 9:30 p.m.

Fee: \$30.00.

Contact: H. M. Walton, M.D., Dean, Graduate School of Medicine, College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33, California.

University of Southern California, Medical Extension Education

Course: Survey Course for General Practitioners.

Date: March 13, 1950, through March 17, 1950, five days, full-time.

Fee: \$50.00.

Place: Los Angeles County Hospital.

Course: Hematology.

Date: March 6, 1950, 12 weekly sessions.

Fee: \$50.00.

Courses in Anesthesia to be arranged. General Review of Clinical Anesthesia; Basic Principles and Techniques. 12 weeks. Tuition \$50.00 to \$300.00.

University of California, Medical Extension

Course: Internal Medicine and General Surgery.

Date: April 24 through 28.

Course: Psychiatry for the General Practitioner.

Date: April 24 through 28.

Contact: Stacy R. Mettier, M.D., Medical Extension, University of California Medical School, San Francisco 22, California. Fee and printed program supplied on request.

Stanford University School of Medicine

Course: Postgraduate conference in Clinical Ophthalmology, March 27 through March 31, 1950.

Registration will be open to physicians who limit their practice to the treatment of diseases of the eye, ear, nose and throat. In order to allow free discussion by members of the conference, registration will be limited to 30 physicians. Instruc-

tors will be Drs. A. Edward Maumenee, Dohrman K. Pischel, Jerome W. Bettman, Earle H. McBain and Arthur J. Jampolsky. Programs and further information may be obtained from Office of the Dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15, California.

Regional Seminar

California Medical Association Postgraduate Activities Committee, the California and the Merced County Tuberculosis and Heart Association Seminar on Heart Diseases will be held at the Merced Women's Clubhouse, March 3, 1950, afternoon and evening. The various aspects of diagnosis and treatment of the cardiac diseases will be covered, including the use of ACTH and Cortisone. A portion of the evening session will be devoted to a round-table discussion.

California Cancer Commission

The California Cancer Commission has announced two February refresher courses in neoplastic diseases for practicing physicians and surgeons. One is to be held in Los Angeles, the other in Oakland.

The Los Angeles course, which is to be given with the cooperation of the Tumor Board of the Los Angeles County General Hospital, is scheduled for Sunday and Monday, February 19 and 20. Meetings will be held in the auditorium of the Los Angeles County General Hospital at 1:30 p.m. and again at 7:30 p.m. on both days. In addition to California speakers, there will be three visiting instructors: R. Lee Clark, M.D., professor of oncology, Graduate School, University of Texas; Charles B. Puestow, M.D., professor of surgery, University of Illinois, Chicago; and Michael E. DeBakey, M.D., professor of surgery, Baylor University College of Medicine, Houston.

The Oakland course, which was arranged with the cooperation of the California division of the American Cancer Society, is to be given Wednesday and Thursday, February 22 and 23, in the auditorium of Providence College of Nursing, 390 Central Avenue, Oakland. Afternoon sessions from 1:30 to 5 and evening sessions from 7:30 to 9 will be held both days. The same three visiting instructors who are to address the Los Angeles meetings will also speak at Oakland.

Specialists as well as general practitioners are cordially invited. There will be no registration fee for either course. Financial assistance is being provided by the American Cancer Society as well as the California State division.

The California Medical Association postgraduate seminar held at Modesto January 19 was attended by over seventy physicians from the Stanislaus, San Joaquin and Merced county societies. The speakers were commended upon their presentations. Dr. Edwin G. Clausen, Oakland, pointed out common errors in the diagnosis and surgical treatment of solitary adenomas of the thyroid, painless

jaundice, gastric ulcer, varicose veins and intestinal obstruction. Dr. Fenimore E. Davis, Oakland, discussed refinements in spinal anesthesia, use of curare preparations in general anesthesia and the indications and technique for using intravenous procaine. Observation of the basic principles of surgery in treatment of compound fractures, and the avoidance of introducing foreign body fixation even with the

adjunct of antibiotics, were emphasized by Dr. Douglas D. Toffelmier, Oakland.

Treatment of the bleeding peptic ulcer was discussed at the evening session. Discussing the general and clinical laboratory methods of proper evaluation and care during the medical regimen, Dr. Fletcher B. Taylor, Oakland, emphasized the value of medical and surgical consultation at 12-hour intervals during the critical period. Dr. Arthur J. Hunnicutt, Oakland, who presented the surgical aspects of the problem, pointed out the importance of oxygen therapy, adequate replacement of lost blood and the indications for subtotal gastrectomy for intractable or recurring hemorrhages.

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"Teamwork" is the theme of the 35th annual meeting of the American Association of Industrial Physicians

and Surgeons and four other industrial associations which will be held in the Sherman Hotel in Chicago, April 22-29. Registration during the meeting is expected to exceed 2,000. The four other groups are the American Industrial Hygiene Association, the American Conference of Governmental Industrial Hygienists, the American Association of Industrial Nurses, and the American Association of Industrial Dentists.

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A vacancy exists for a qualified bacteriologist in the pathology laboratory of the Veterans Administration Center, Los Angeles. The position pays \$6,400 a year. Qualifications for the post are shown on Standard Form 57, which can be secured at any post office. Applications on Form 57 should be sent to the Personnel Officer, Veterans Administration Center, Los Angeles 25.



BOOK REVIEWS

A MANUAL OF THE PENICILLIA. By Kenneth B. Raper, Principal Microbiologist, Fermentation Division, Northern Regional Research Laboratory, Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture, Peoria, Illinois; and Charles Thom, Collaborator, U. S. Department of Agriculture. The Williams and Wilkins Company, Baltimore, Md., 1949. \$12.00.

Species of Penicillia are among the most common of the fungi not pathogenic for man and animals. These molds occur widely in nature but attracted relatively little interest until one of them was demonstrated by Fleming to produce penicillin. The discovery of this substance and the search for improved methods of production led to a complete re-examination of the Penicillia.

This book represents the results of this study, and classifies and describes this genus in the greatest detail. The work is of no interest to physicians but will be very valuable to those scientists whose work requires an understanding of these fungi.

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X-RAY TREATMENT—ITS ORIGIN, BIRTH AND EARLY HISTORY. By Emil H. Grubbe, B.S., M.D., F.A.C.P. The Bruce Publishing Company, St. Paul, 1949. \$3.00.

This is an interesting monograph of 154 pages written by a Chicago physician of some 50 years' experience in medical practice. The author sincerely believes that he was "the first person in the world to actually make use of these rays in the treatment of disease." He sustained injury to his own hands while working with the rays in 1896 and states that he thereafter applied the rays to a number of patients in the hope of obtaining effects.

The photographs of the author's laboratory in the earlier days of this century, and of the general lecture room in the "Illinois School of Electrotherapeutics" will bring back memories of early physics laboratories to many readers.

Appended to the book is the author's biography including a summation of the ten "firsts" to his credit. It is suspected that some early workers with radiant energy in Europe and South America will contest several of these firsts. Nevertheless, the biographic notes are of considerable interest and reveal to the younger generation the kaleidoscope of medical schools in the Chicago area during the last several decades.

The monograph can be recommended as light reading to those interested in radiation therapy, and in the history of this particular division of medicine.

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RATIONAL MEDICINE. By John W. Todd, M.D. (Lond.) Assistant Physician to Farnham Hospital. The Williams and Wilkins Company, Baltimore, 1949. \$6.50.

In 1943 Dr. Todd was sent from England to Asia for a three-year stay which gave him a chance to sit and think, and to consolidate his ideas on his profession. The result, this book: The thoughts of a sensitive and analytical mind on the application of modern medicine to the patient. It is the sort of book which can be written without using a single reference. It is filled with the rebellious philosophy of a conscientious spirit. In it the author jousts at many of the accepted complacencies and fallacies of today's medicine as well as yesterday's. It is a provocative book, calculated to irritate the smug among us.

The book follows, in considerable part, the outline of a textbook of medicine. But the author gives a minimum of

data with a maximum of analysis and reasoning. In each chapter, he presents his own ideas on the purpose of the procedure considered. He repeatedly emphasizes the emotional and social sides of an illness along with its physical aspects. At the same time he argues that past psychological evidence should be evaluated in much the same way as past organic evidence. He consistently points out the inadequacies, falsities, pomposities, and limitations of certain time-honored symptoms, signs and tests. He deplores over-simplification (but at times has this very fault, e.g., in the treatment of peptic ulcer on page 204).

His viewpoint is probably best summarized by the following quotation (page 310): "Until the day dawns when the ideas are accepted that man is an indivisible whole, that psychiatry permeates the whole of medicine, and that students should be taught by the same men at the same time and on the same patients about the disorders of the mind as about the diseases of the body, it is to be feared that the misunderstanding of the relations between mind and body will continue."

The book can be highly recommended to all doctors who are not afraid to look at themselves or at their profession, critically and philosophically.

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STERN'S APPLIED DIETETICS—The Planning and Teaching of Normal and Therapeutic Diets. Revised by Helen Rosenthal, B.S., Chief of Frances Stern Food Clinic, the Boston Dispensary, Assistant in Medicine, Tufts College Medical School; Pearl C. Baker, B.S., former Associate, Frances Stern Food Clinic; and Wilma A. McVey, M.D., Assistant in Medicine, Tufts College Medical School. Third edition. The Williams and Wilkins Co., Boston, 1949. \$5.00.

This volume outlines the procedure of the food clinic of the Boston Dispensary for the planning and teaching of normal and therapeutic diets. As such, it meets the particular problems which are encountered in this kind of clinic. The techniques described may be satisfactory for filling the food prescriptions for an out-patient department, but they are less suitable for use in the private practice of medicine.

The book is written essentially for the dietitian, the social worker, and the health educator working with a dietitian. The doctor of medicine will find it, for the most part, on a different level from his usual sources. However, Part II and Part III may prove of some value to him: Part II is made up of tables which simplify the computation of diets; Part III is composed of dietary outlines which summarize the purposes and construction of different types of diets. These make a reference which may fit on a physician's shelf.

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TEXTBOOK OF OPHTHALMOLOGY, Vol. IV—The Neurology of Vision Motor and Optical Anomalies. Sir W. Stewart Duke-Elder, K.C.V.O., M.D., Ch.B., F.R.C.S., Surgeon Oculist to H.M. the King, 1081 illustrations, including 71 in color. The C. V. Mosby Company, St. Louis, 1949. \$20.00.

The fourth volume of this series is like its predecessors, an excellent text and reference book.

The book has a carefully outlined contents. The book itself contains 13 chapters and 1,123 pages of subject matter.

The chapters on the lesions involving the visual pathways and the field studies in these cases are very well done and very readable. The organization of the symptoms, the typical lesions with careful field studies, makes this portion of the

book of interest to the neurologist as well as the ophthalmologist.

Chapter XLIV on pupillary pathways and anomalies is especially well done and excellent reading.

Chapter XLVII to Chapter L on the problems of squint is especially comprehensive. The subject is exhaustively covered from an etiological standpoint. The chapter on non-comitant squint includes every conceivable causative factor including the various diseases, and the various drugs and poisons which may have been ingested.

Chapter LI upon errors of refraction has a very clear-cut and logical discussion of myopia which every ophthalmologist should carefully read.

In conclusion, this volume like its predecessors should be in every ophthalmological library.

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ROENTGEN DIAGNOSIS OF DISEASES OF THE SKULL. By Max Ritvo, M.D.—*Annals of Roentgenology*. Paul B. Hoeber, Inc., New York, 1949. \$16.00.

The flow of volumes on the roentgen diagnosis of disorders of the head and neck continues unabated. The present volume of approximately 400 pages contains about 370 illustrations, many of them of good quality. The text is clear and not crowded. There are chapters on the x-ray examination of the skull, on the various anomalies, traumatic and postoperative changes, and the infections. Then follow chapters on endocrine and metabolic disturbances, the status of the skull during pregnancy, intracranial opacities of various types, neoplasms and finally cerebral angiography.

The legends under some of the illustrations need revision in the next edition. For example, Figure 261 is described as "aeration of the dorsum sellae" when actually it is a case of calcification of the retrosellar dura. There should be additional close-up reproductions of the sella in the chapters devoted to that portion of the skull. The detail in many of the existing illustrations is not sufficiently clear.

This reviewer trusts that in subsequent editions the use of personal names applied to simple processes will decrease. For example, on Page 342 the author has a short section on "Schmincke tumors." He also uses the synonym "lymphoepitheliomas." It might be simpler to use the term nasopharyngeal carcinomas (transitional type).

The volume can be recommended for the libraries of roentgenologists and neurologists.

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MODERN PRACTICE IN PSYCHOLOGICAL MEDICINE—1949. Edited by J. R. Rees, M.D., Paul B. Hoeber, Inc., Medical Book Department of Harper and Brothers, New York, 1949. \$10.00.

This apparently is intended as a text in psychiatry (or psychological medicine, if you will) for the medical student. It consists of contributions by over a score of authors, specialists in the various fields that have greater or less association with the subject. In common with all such works, it gains from the special knowledge of the individual contributors while losing perhaps more than commensurately by the disjointedness inherent in multiple authorship. To this reviewer it appears neither intensive enough for the serious student of the specialty, nor well enough systematized for the newcomer.

The initial chapter, entitled "Health," should be read by physician and layman as well, since it gives clearly and briefly one present concept of psychiatry. This apparently is that the human race is headed for extinction unless those trained in psychological medicine are given an opportunity to overhaul the human nature, ridding us of our hostilities and aggressions, and thus making wars a thing of the past. This psychiatric pipe-dream is not something to give us any great regard for the common sense of the spokesmen of the specialty.

An excellent chapter on neurology seems rather lost in the middle of the book, while the concept of venereal disease as a psychosomatic entity is novel if not entirely orthodox. In all, the book, which is published in England, is of interest to the psychiatrist, but can hardly be recommended as a text for the medical student.

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ORAL BACTERIAL INFECTION—Diagnosis and Treatment. By Lyon F. Streat, M.Sc., Ph.D., D.D.S., F.A.P.H.A., Director of Research, Novocel Chemical Mfg. Co., Inc. With 57 illustrations. Dental Items of Interest Publishing Company, Inc., Brooklyn 7, New York, 1949. \$5.50.

This book adds little to the general advancement of the science of bacteriology or to the arts of diagnosis and treatment. Its title and date of original publication suggest a rather complete treatise on oral bacterial infections as well as their diagnosis and treatment, yet not much is recorded therein that deals with infections in the mouth. No mention is made of "strawberry" tongue in scarlet fever. No attempt is made to provide adequate descriptions of Koplik's spots of rubeola and the oral lesions in gonorrhreal stomatitis, infectious stomatitis, epidemic stomatitis and mycotic stomatitis. The oral manifestations of diphtheria, syphilis, and anthrax are poorly covered. The book, however, does give a fair account of ulceromembranous gingivitis. Because of these important limitations the book is not of great value as an aid in the diagnosis of oral bacterial infections.

The volume is essentially a summary of medical bacteriology. The author discusses briefly the staining and culturing of bacteria, sterilization techniques and the morphology of bacteria. He skims over the pyogenic cocci, the diphtheria organism, the tubercle bacillus, the colon-typhoid dysentery group and other pathogenic bacteria. He deals briefly with the antibiotics and immunity and offers little information about the pathogenic fungi, the protozoa and the filterable viruses.

In the preface it is stated that the author intends this book "... as a text for medical and dental students preparing for final examinations and for the general practitioner requiring certain basic information quickly and cannot avail himself of the facilities of a medical library." The reviewer cannot agree that the book will serve well for preparing medical or dental students for final examinations.

Surely the thoroughness with which these important courses are now being taught in our medical and dental schools suggests reference books that are considerably more complete than the book now under consideration through this review. The volume can be of use to dental assistants or laymen who desire superficial information on medical bacteriology.